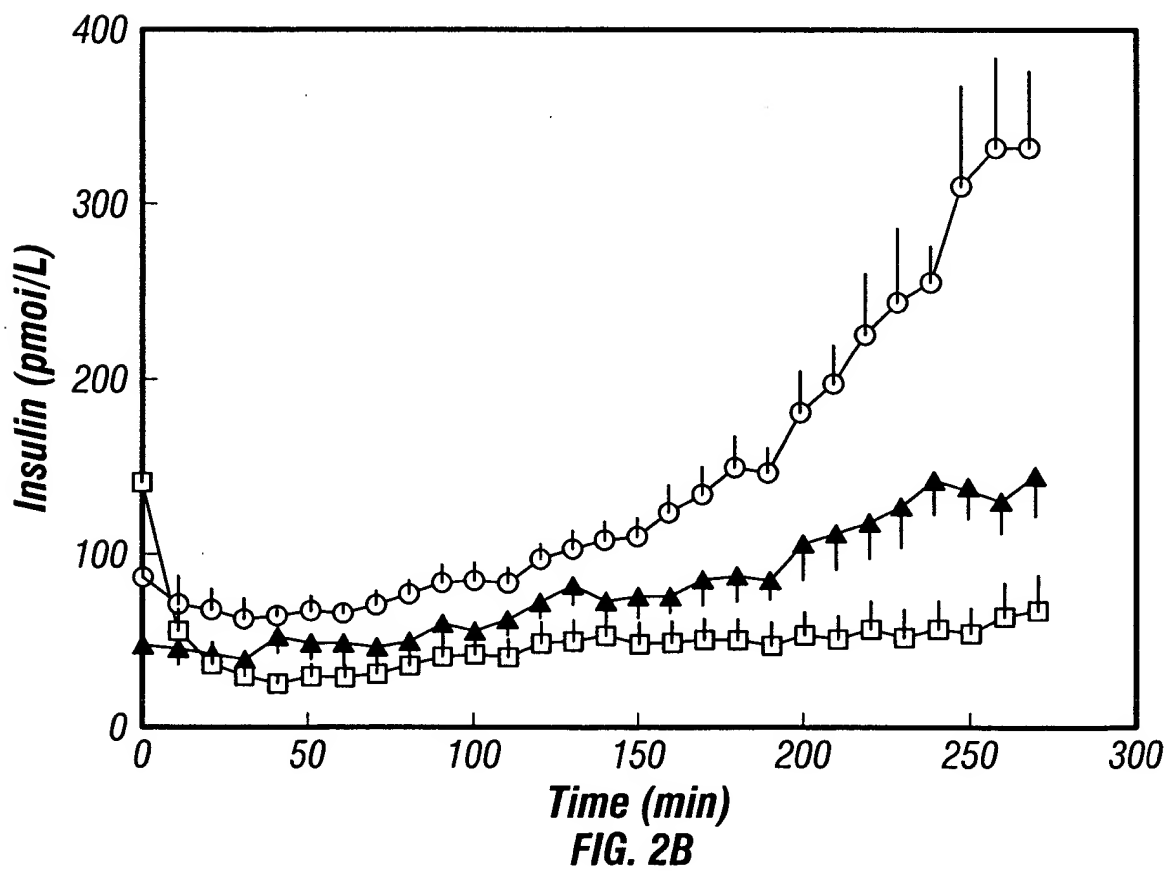
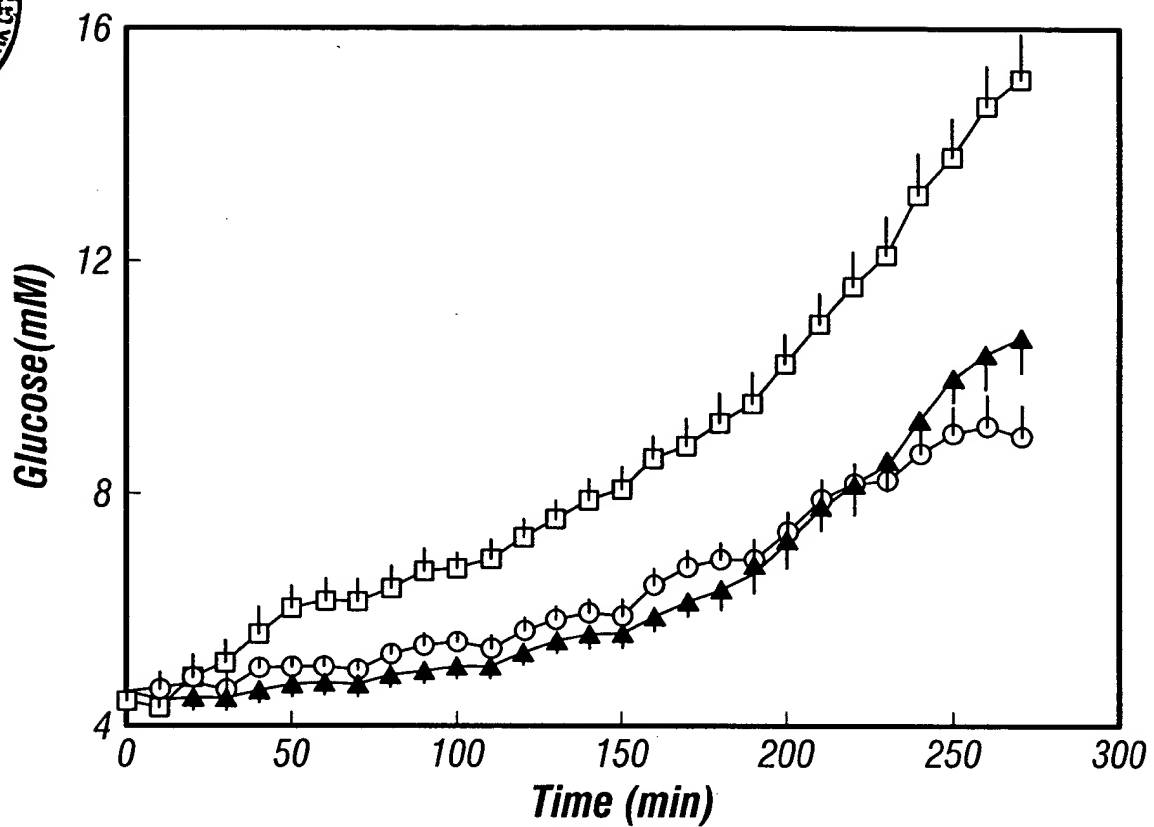


FIG. 1



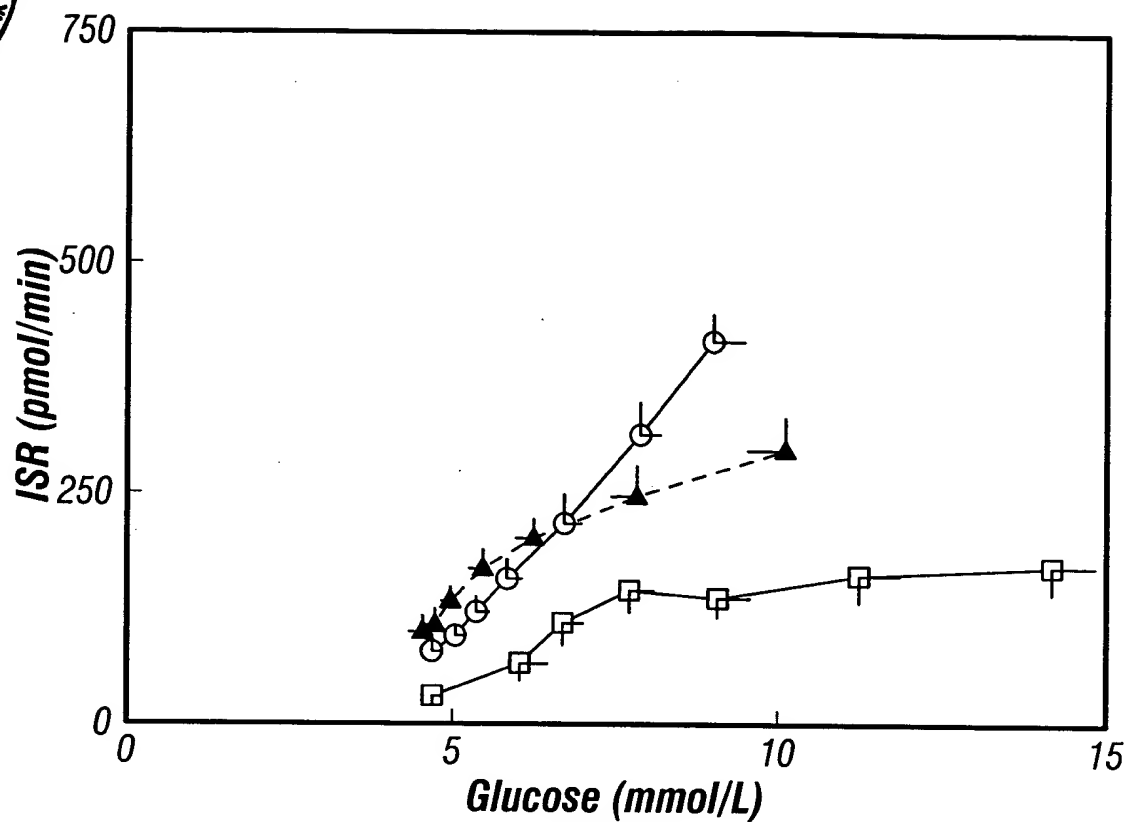


FIG. 3

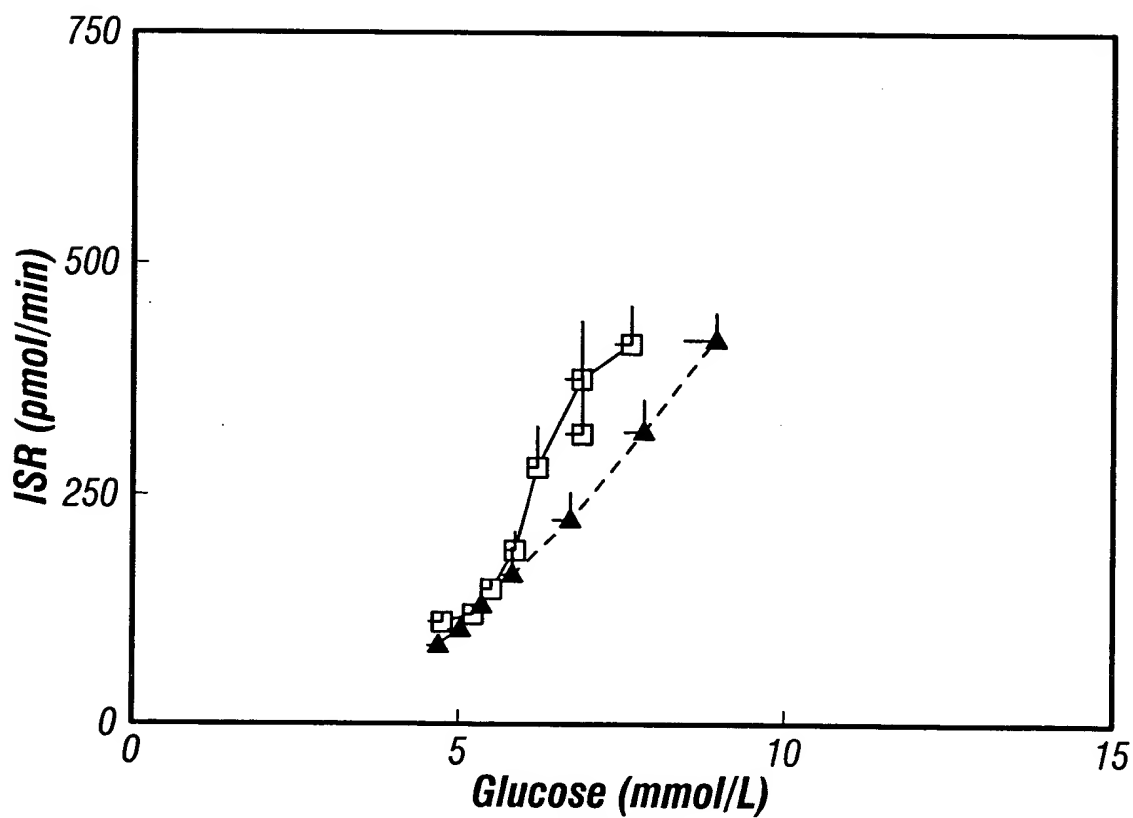


FIG. 4A

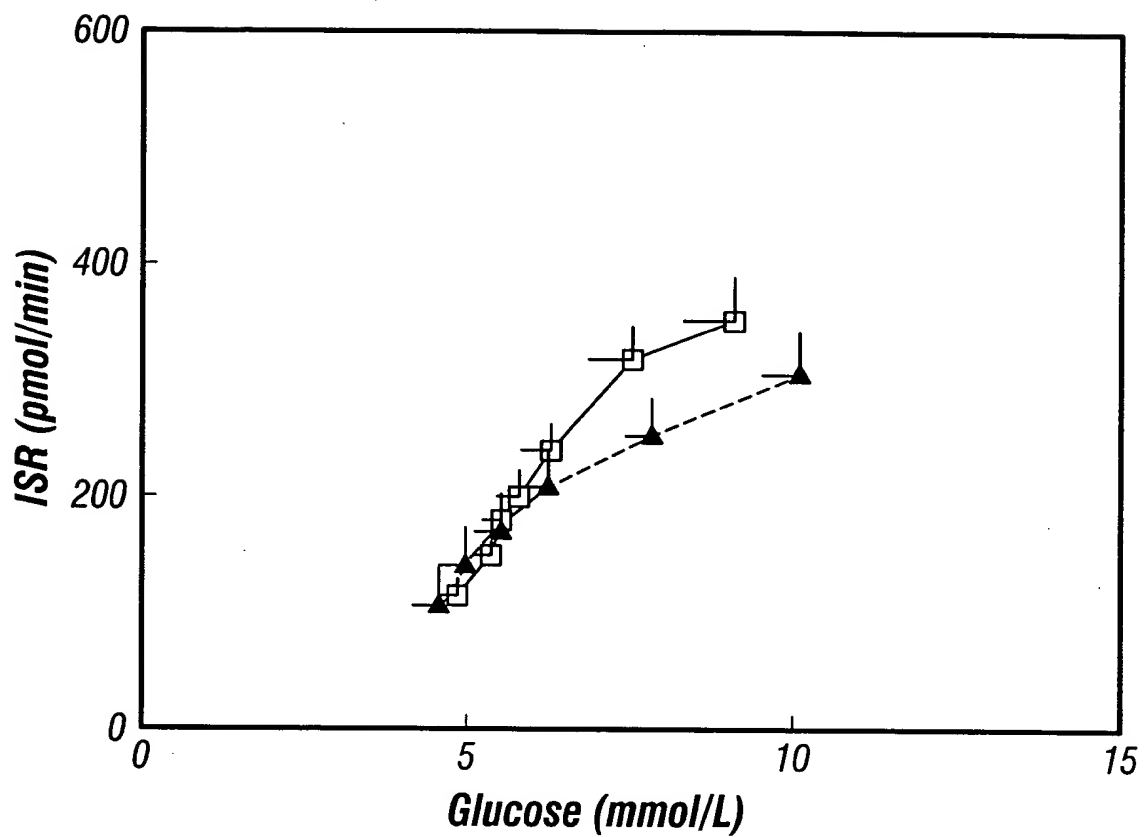


FIG. 4B

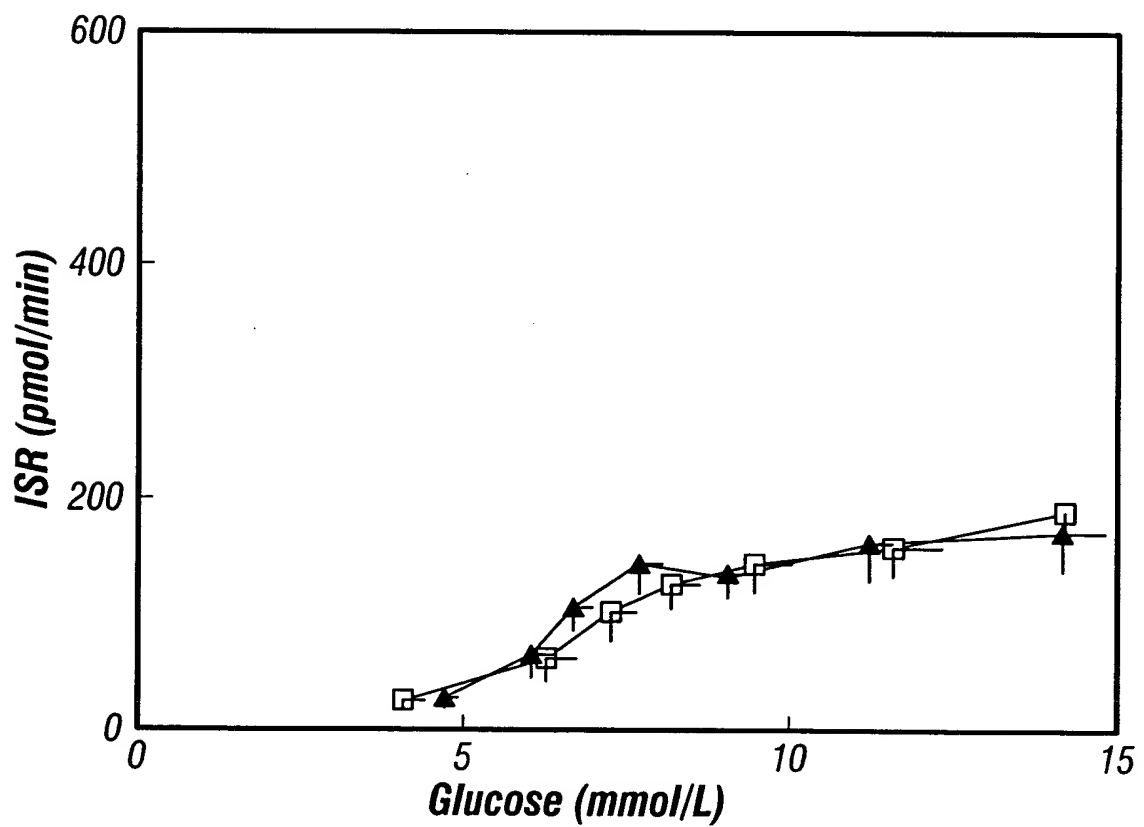


FIG. 4C

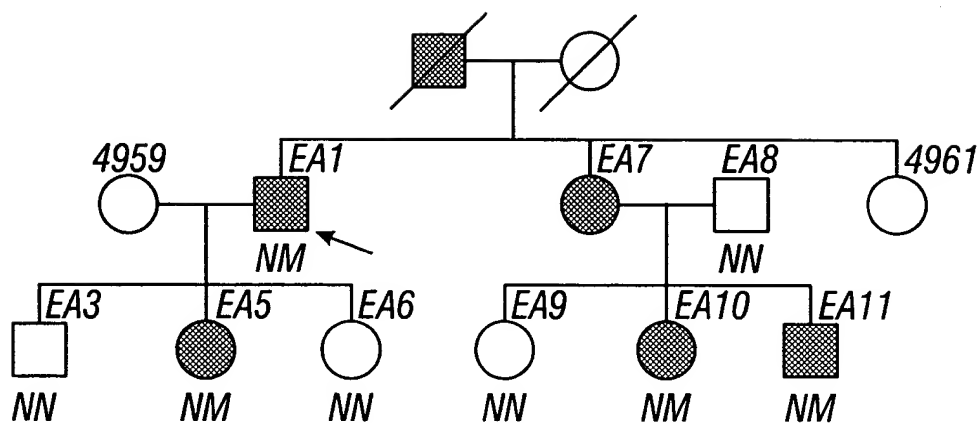


FIG. 5A

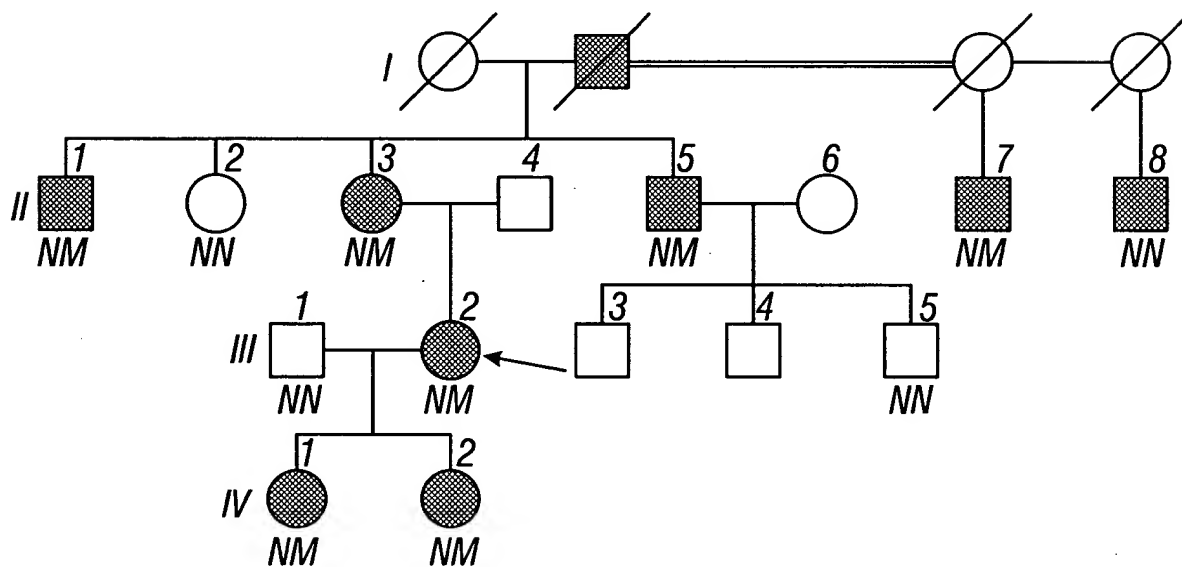


FIG. 5B

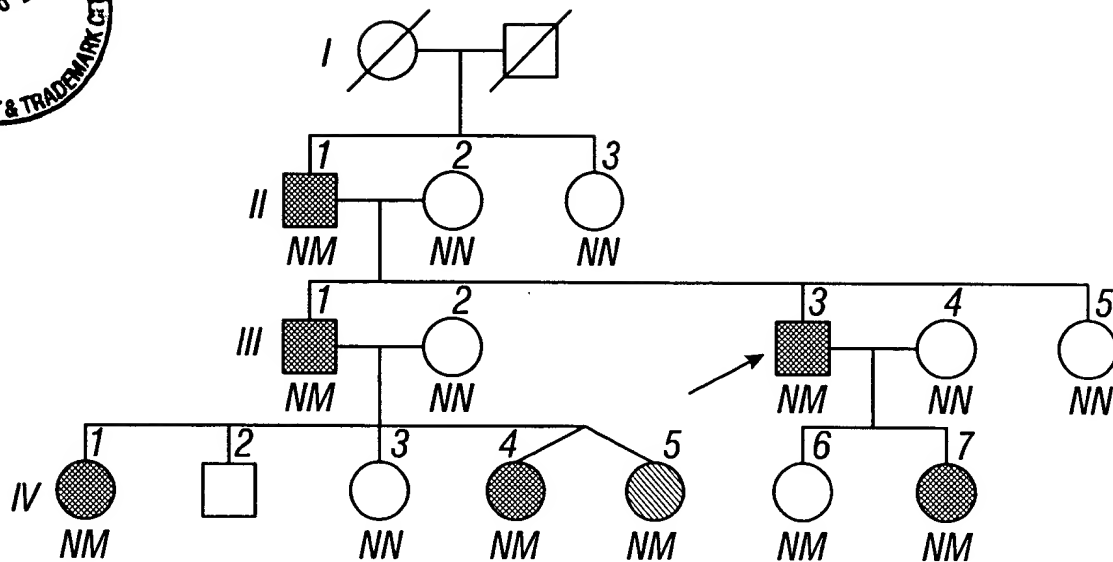


FIG. 5C

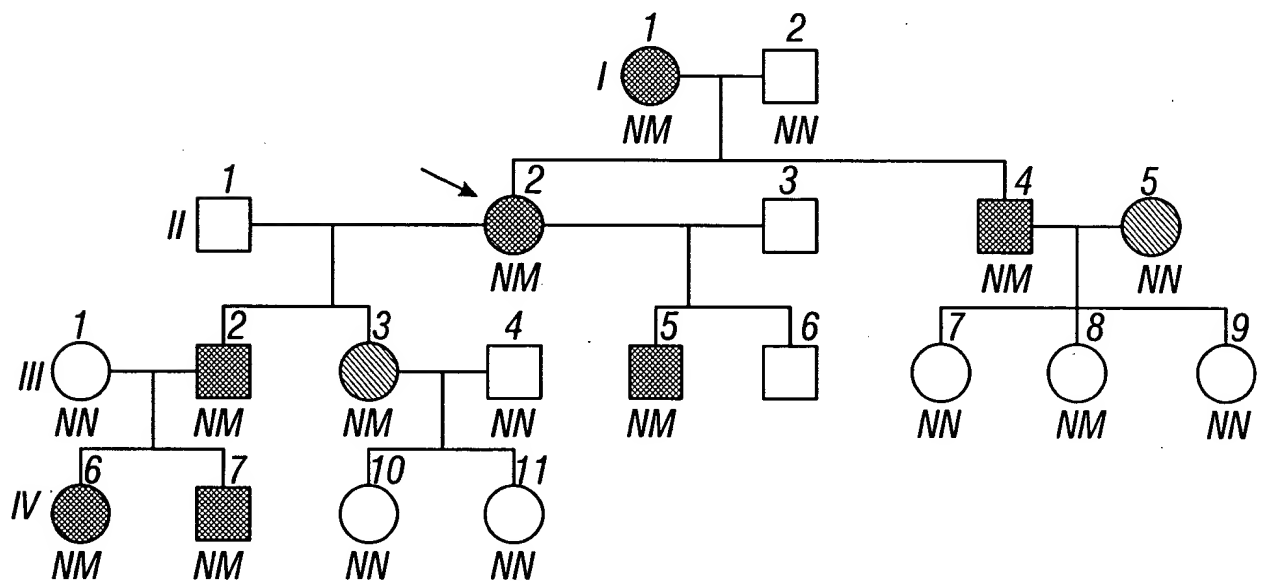
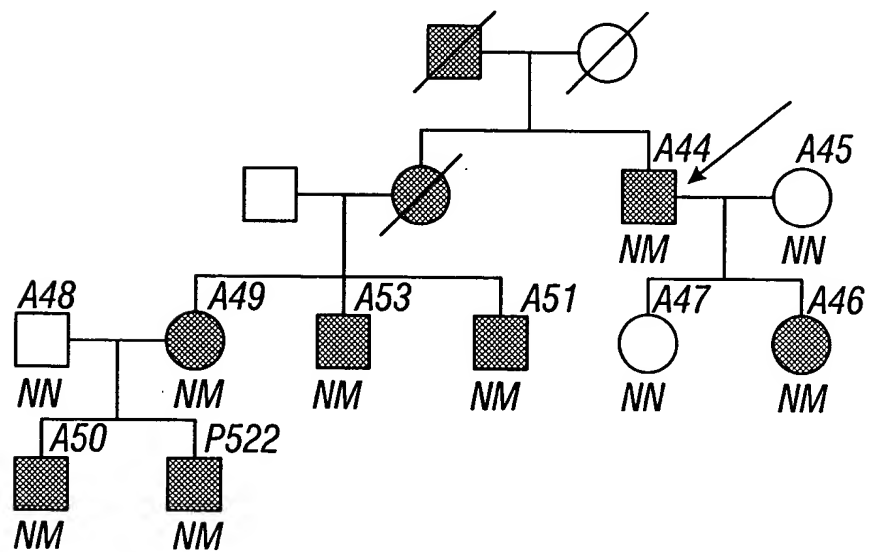
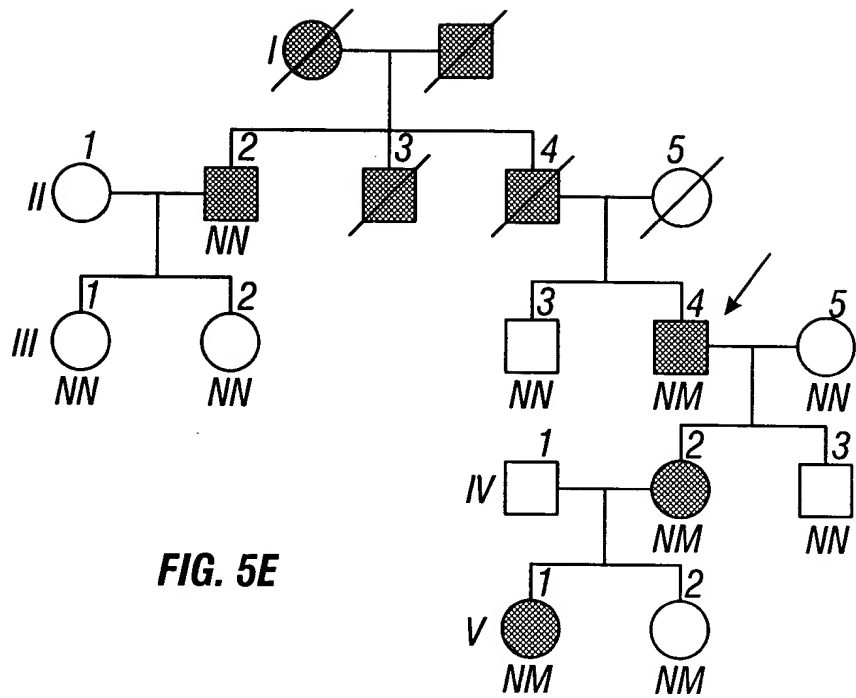


FIG. 5D



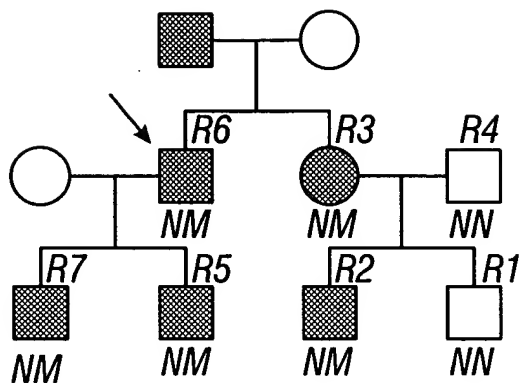


FIG. 5G

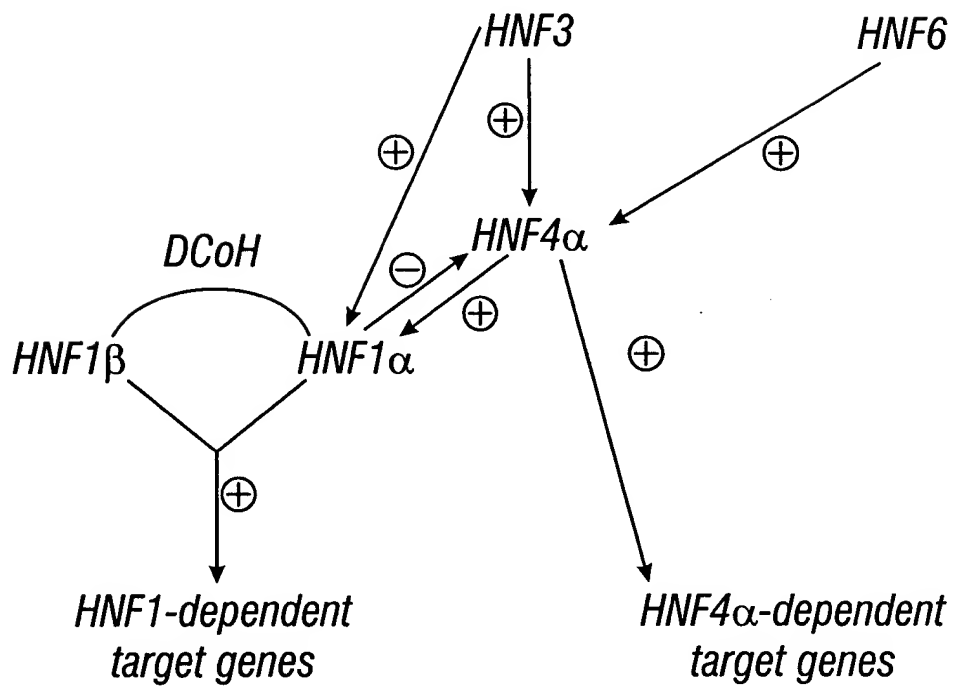
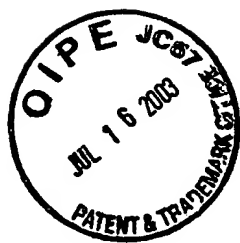


FIG. 6



MARK 0710X

		Majority									
		10	20	30	40	50	60	70			
M-----D-DMADYSAALDPA		TLEFENVQVLTMGNDL-----L-----G-----G-									
1	MRLSKTLV	DMADYSAALDPAYTTLEFENVQVLTMGNDLLPLRLARLRHPLRHHSI-SGGVDSSPQGD									
1	M-----	DMADYSAALDPAYTTLEFENVQVLTMGND-----									
1	M-----	DMADYTEALDPAYTTLEFENVQVLSIGTD-----									
1	MH-----ADALASAYPAASQPHSPI	-----GLALSPMGGL-----GLSNSSNQSSNFALCNGNGNAGSAGG									
TSPSEGTN-----		LNASNSLGSVLSALCAICGDRATGKHYGASSCDGCKGFF									
70	TSPSEGTN-----	LNAPNSLGSVLSALCAICGDRATGKHYGASSCDGCKGFF									
31	TSPSEGAN-----	LNSNSLSVLSALCAICGDRATGKHYGASSCDGCKGFF									
31	TSTSDVTS-----	LSASNSLGINSLCAICGDRATGKHYGASSCDGCKGFF									
59	GSASSGNNNNMFSFYNNLNGSGGTNSSQQQLQQQQQQSPVCAICGDRATGKHYGASSCDGCKGFF										
RRSVRKNHMYSCFRSQCVVDKDRNQCRYCRLKKCFRAGMKKEAVQNERDRISTRSSYEDSSLP---S											
115	RRSVRKNHMYSCFRSQCVVDKDRNQCRYCRLKKCFRAGMKKEAVQNERDRISTRSSYEDSSLP---S										
76	RRSVRKNHMYSCFRSQCVVDKDRNQCRYCRLKKCFRAGMKKEAVQNERDRISTRSSYEDSSLP---S										
76	RRSVRKNHMYSCFRSQCVVDKDRNQCRYCRLKKCFRAGMKKEAVQNERDRISTRSSYEDSSLP---S										
129	RRSVRKNHMYSCFRSQCVVDKDRNQCRYCRLKKCFRAGMKKEAVQNERDRISTRSSYEDSSLP---S										

FIG. 7A



QIQFIKLFGMAKIDNLLQEMLLGGSASDAP-----HTHHPLHP-----										Majority
430	440	450	460	470	480	490				
384 QIQFIKLFGMAKIDNLLQEMLLGGS	PSDAP				HTHHPLHP					hHNF4-a-protein
345 QIQFIKLFGMAKIDNLLQEMLLGGS	ASDAP				HTHHPLHP					mHNF4-protein
344 QIQFVKLFGMAKIDNLLQEMLLGGS	ANEAS				HTHHPLHP					X.LavesHNF4-protein
409 QIQFAKIFGV	AHIDSL	QEMLLGGE	LADN	PLSPPNQ	SNDYQS	PTHTGN	MEGGNQ	VNSSLD	SLATSGGP	Drosophila HNF4

FIG. 7B-2



Majority

-----HLMQEHM-----	500	510	520	530	540	550	560
-----HLMQEHM-----	422	-----HLMQEHM-----	-----HLMQEHM-----	-----HLMQEHM-----	-----HLMQEHM-----	-----HLMQEHM-----	-----HLMQEHM-----
-----HLMQEHM-----	383	-----HLMQEHM-----	-----HLMQEHM-----	-----HLMQEHM-----	-----HLMQEHM-----	-----HLMQEHM-----	-----HLMQEHM-----
-----HLMQEHM-----	382	-----HLMQEHM-----	-----HLMQEHM-----	-----HLMQEHM-----	-----HLMQEHM-----	-----HLMQEHM-----	-----HLMQEHM-----
-----HLMQEHM-----	479	-----HLMQEHM-----	-----HLMQEHM-----	-----HLMQEHM-----	-----HLMQEHM-----	-----HLMQEHM-----	-----HLMQEHM-----

hHNF4-a-protein
mHNF4-protein
X.LavesHNF4-protein
Drosophila HNF4

Majority

-----GQAATPETPQPSPPP-----	570	580	590	600	610	620	630
-----GQAATPETPQPSPPP-----	455	-----GQAATPETPQPSPPP-----	-----GQAATPETPQPSPPP-----	-----GQAATPETPQPSPPP-----	-----GQAATPETPQPSPPP-----	-----GQAATPETPQPSPPP-----	-----GQAATPETPQPSPPP-----
-----GQAATPETPQPSPPP-----	416	-----GQAATPETPQPSPPP-----	-----GQAATPETPQPSPPP-----	-----GQAATPETPQPSPPP-----	-----GQAATPETPQPSPPP-----	-----GQAATPETPQPSPPP-----	-----GQAATPETPQPSPPP-----
-----GQAATPETPQPSPPP-----	409	-----GQAATPETPQPSPPP-----	-----GQAATPETPQPSPPP-----	-----GQAATPETPQPSPPP-----	-----GQAATPETPQPSPPP-----	-----GQAATPETPQPSPPP-----	-----GQAATPETPQPSPPP-----
-----GQAATPETPQPSPPP-----	549	-----GQAATPETPQPSPPP-----	-----GQAATPETPQPSPPP-----	-----GQAATPETPQPSPPP-----	-----GQAATPETPQPSPPP-----	-----GQAATPETPQPSPPP-----	-----GQAATPETPQPSPPP-----

hHNF4-a-protein
mHNF4-protein
X.LavesHNF4-protein
Drosophila HNF4

Majority

-----KQEA-----I	640	650	660	670
-----KQEA-----I	477	-----KQEA-----I	-----KQEA-----I	-----KQEA-----I
-----KQEA-----I	438	-----KQEA-----I	-----KQEA-----I	-----KQEA-----I
-----KQEA-----I	428	-----KQEA-----I	-----KQEA-----I	-----KQEA-----I
-----KQEA-----I	619	-----KQEA-----I	-----KQEA-----I	-----KQEA-----I

hHNF4-a-protein
mHNF4-protein
X.LavesHNF4-protein
Drosophila HNF4

FIG. 7C



Partial Sequence of Human HNF4 Gene
(Exon 1, SEQ ID NO:34)

GCAGAGAGGG	CACTGGGAGG	AGGCAGTGGG	AGGGCGGAGG
GCGGGGGCCT	TCGGGGTG	CGCCCAGGGT	AGGGCAGGTG
GCCGCGGCGT	GGAGGCAGGG	AGAATGCGAC	TCTCCAAAAC
CCTCGTCGAC	ATGGACATGG	CCGACTACAG	TGCTGCACTG
GACCCAGCCT	ACACCACCCT	GGAATTTGAG	AATGTGCAGG
TGTTGACGAT	GGGCAATGGT	AGGTGGGGGC	AGATGTGCCC
AGGTGTGCCA	GTGGGGGCAG	GTGTGCCTGG	GTCCAGGAGC
AGATCTTTGG	CACTCAACTT	TGGGGTGGGA	GGAGAATGAT
ACAAAATGGT	AGGTTGGTCC	TACAGGCCAG	CACAGGTGTT
GCCAAGTGAA	GCCCATGTGC	CCAGGCACAG	TGATCACAGG
CATTCTGGGT	GAAGGGAGGC	CTGCAAGGGC	CAATTTCCAG
CAAAAGTCGA	TCCCGGCTAT	TCCTCCCAGG	CCCTTCCAGT
CCTCACTGCC	TCACAGTGGC	TCTGCTTGGC	GCTTGGCACA
GTGACATGAT	GGTGAGCTCC	CCCTTGGTGC	CCAGCTCCAG
CGATTCAGCC	CAGCACGGCC	CCTTCGTGAA	CCCCTTGGGC
CTAGGTTCAG	AGAGACGGCA	AGGGATGTTG	TATCCCTGGA
GATGGTGGTT	GGAGACATAA	CCGCATTTCT	C

FIG. 8A



Partial Sequence of Human HNF4 Gene
(Exon 1b, SEQ ID NO:36)

TGGATGTTTG	TACATGTGTG	CTGTGTGTGC	GGGTCATAGA
GCACATGTGT	TTGTGCATGC	GGACCTGTTG	GAGTGCCCTG
TTCTTCCTGC	ATCTTTATCC	TGTATGGGCG	TTTTGTCGTG
TGCCCATATT	TGTACCTGCT	GTGTATATAT	GCAGTTCCCT
GTGCTGCGGG	CGGGGGTCAG	CGGTCTCTGG	TGTGCACGAC
TGCACAGACC	CAAATGCAGG	ACTCTGTTGT	TGCCACTCAC
CAAGTGAGAT	TCATATCAGC	AACATGTCCG	TTTGTCTCTG
AGCAGATTTG	TTGCCGCTGC	GTCTCGCCAG	ATTGAGGCAT
CCCCTCCGAC	ATCACTGGAG	CATATCTGGA	GGGGTGGACA
GTTCTCCACA	GGGAGGTAGG	GGAAAAGAGG	AGGCCCGGAA
ACCCCTCCTG	GAGGGAAGAG	CCCCATCGGT	CCCAGGCCAG
CCTCAGAGGA	GAGGGGGCAG	GCAGCTGGCT	GAGGTCAGCC
TYGCCACCCTG	CTTCCTTCTG	TGTCTTGGAG	CCACTCAGCC
AGTATGAGGC	TGCAGCTCCA	GCTGAGGTCT	GGAATCTTGT
GGTCAGCTCA	GCTAGGGTGA	GGAGGCAGCT	GCTGGGCACT
GCTTGTTGTC	AGCTCAGCAG	GTGCTCACCT	GCCCCTGCCG
TCCAGTCACG	TGTCACCTTG	GGCATGTCAC	CTCCCCTATC
CTGGCTTCTG	TATCTTCTAC	AAAACAGGCT	TCATTCCCCC
AGGCCTGCTG	GCTGGACGGC	TTTTAGGCCT	GTCTGAGGAC
CACGCCAGGA	GCGCAAGGCA	AAAACACACC	AGAGAT

FIG. 8B



Partial Sequence of Human HNF4 Gene
(Exon 2, SEQ ID NO:38)

CCCCTTGCGA	GTTAGGAGGC	CGGCTCCCAC	CCCAGAAGGT
GGCCAGGTTT	TCATGCCTTC	CTAGAGAAAG	CTGGGGCTGG
TGGCCTCCAC	CACAGGGAGA	CGCAGACCCT	CAGAAACAAG
TCTGTGAAGT	CACAACCAGC	CCCAGTTTAC	AGATGTGAAA
CTGAAGCTCC	AAAAAGTCAG	GAGGTCACTG	AGTGGGGAGG
TGATGGAGTG	GAACAGCCCC	CAGATCTGGC	TGAGGCCGAA
GCCCTGGAGA	GATCCCCGCA	AGGCTCCCTT	AGATGCCTGA
CATTCTGTTC	TTCCTGAAGC	CTCACTCCCT	TCTCTCCTGG
CGCAGACACG	TCCCCATCAG	AAGGCACCAA	CCTCAACGCG
CCCAACAGCC	TGGGTGTCAG	CGCCCTGTGT	GCCATCTGCG
GGGACCGGGC	CACGGGCAAA	CACTACGGTG	CCTCGAGCTG
TGACGGCTGC	AAGGGCTTCT	TCCGGAGGAG	CGTGCGGAAG
AACCACATGT	ACTCCTGCAG	GTGAGGAGCC	TCAATTTCTT
CAGCTGGGAA	ATGGGCACAC	TTGGGCTCAT	GGCCCCAAGG
TCTGTCTTCT	CCCTGAGTGG	GTAGGTCCCA	GAGACAGCTG
CCCTTCAGGG	CCTTCAAGGC	TCCTTCTGGTT	TTGT

FIG. 8C



Partial Sequence of Human HNF4 Gene
(Exon 3, SEQ ID NO:40)

AGAGAGTTCA	TAGCACCTTT	CCAGCTCCTG	GTGGGTTCAA
GAGAGAACTC	CCGGGATGAA	GAGATGAGAG	CACTGAGGTT
GGGGGGTCAA	CTGGATAGCC	AGGGCCCTAG	TTCTGTCCTA
AGAGGAGGAA	GTTGTGTCTT	CTCCATCCAA	CCATCCAAAAG
ACCTCCCCAG	ATTTAGCCGG	CAGTGCGTGG	TGGACAAAGA
CAAGAGGAAC	CAGTGCCGCT	ACTGCAGGCT	CAAGAAATGC
TTCCGGGCTG	GCATGAAGAA	GGAAGGTGAG	CCTCGGCCCT
CCCCGCCCCA	CCACCCTGCT	ACCACCTGCA	CCCACAGCTC
CCCGACAGTC	ATTTACAAC	GTAGCCACAC	TTTATGACTC
AGTGGCAGGC	CCCAGGGTGA	CTGGCTAATG	GCTGAGAAGA
GGGAGGGCCT	GGAAATCTGA	CCATAGGGAG	CGGCTGGGCT
TGGTCTTGAG	AAAGATTC		

FIG. 8D



Partial Sequence of Human HNF4 Gene
(Exon 4, SEQ ID NO:42)

```
tcccactcct catcagtcac agacaccccc accccctact
ccatccctgt tctccctcct cacctctctg tgcctcctca
cagCCGTCCA GAATGAGCGG GACCGGATCA GCACTCGAAG
GTCAAGCTAT GAGGACAGCA GCCTGCCCTC CATCAATGCG
CTCCTGCAGG CGGAGGTCCT GTCCCGACAG GTACCGGGGT

GATCCTGCCA CCCACCCAGG GGATCCCCCA CACTACAGAG
GAGCTCACCT CCTCCACCTC CATTCTCCCC AGCCAGGCCC
TGGAGCAGCT GACGGGAGGG GCCTCAGATA TTACAGAAGG
GACACTGAGT GCGGTTTCAC ATGGCCCAGT TTGCAGCAAG
GGCAGGAATC GAACCTGGCG CCCTGGGGCA CTTTCTAATT

CATCCTACTG CCTGCATCCC ACAGGCCAAG CAGAGTCTTC
ACCTTCACTG AGGGCCTGCG ATCAGCTCAG CTCCGAGAGA
ACAGAGCAGT GGCTCAGTGG AGAGAGGTGG CAAAGTGGGG
CCCAGCCCTT CCCTTGCTGA GTGACCTTGG GCAAGTCACA
GCACCTCTCT GAGCCATGGT TGCCTCATTG TCAGAAAAGG

ATGATGATTT TTTGCCTGC TTCTCCTCTA AGGCTGACAG
ACTCCTTGGG GCTCTAAAGC TG
```

FIG. 8E



Partial Sequence of Human HNF4 Gene
(Exon 5, SEQ ID NO:44)

```
TTCTCCTCA TCCCTGCCTC CTCCCTCCCT CCGTTTTTAC
CCTGAGCTTC CTTCAGAGCT GGAGGGCACC CACTATCCAG
CCCCCTCCCC ACATCTGATT CCAGGGAGGG GGCTCTGTGC
AGGGGACAGA GAATGCGGGA GGGCCCGGAC ATCTCCAGCA
TTTTCTTCCC TGTATCTCTC GAAGATCACC TCCCCCGTCT

CCGGGATCAA CGGCGACATT CGGGCGAAGA AGATTGCCAG
CATCGCAGAT GTGTGTGAGT CCATGAAGGA GCAGCTGCTG
GTTCTCGTTG AGTGGGCCAA GTACATCCCA GCTTTCTGCG
AGCTCCCCCT GGACGACCAG GTGAGGATGG GCGTGGATGG
TGGGCAGTAG TGGGCAGTGG GCGGGGCAGC CAGGGGGCTG

CTGGCCCACC TGGGATATAG CCGTGGACTG GCTTGATTTT
ATTTTATTTA ACAAATATG TAGTGCACAC ACGTGTCTGA
AACTTTAAAT CACCTTACAA ATATTAAGTC AGTTAGCTCC
TCCAACAACCT CTATGAGGTA GGTACTAAGG TACTATTATT
ACTGCCATCT CATAGGTGAG AGATTGGGGC ACAGAGAGGT

TAAGTAACCT GCTCAAGGTC ACATAGCTAC TATCCAGCAT
AGCTGGG
```

FIG. 8F



Partial Sequence of Human HNF4 Gene
(Exon 6, SEQ ID NO:46)

ATTTTACAA	AGCACCTTC	ATAATTCTCC	ATAGCTGGTC
CATGGGTGGG	AATTTGGGAC	CCACAGTTTT	GGAACTTTTT
GGGATCATAG	ACCTTTTTGA	GAATCTCAAA	AAAGAAAAAA
AAGCACACAG	AATGTTGCTT	ACAGTTTCAT	CAGGCACACA
GAAGAGGCCC	AGCACGAAGC	AGTTTCTTGC	CCAAGGACAC
AGCAGTTCAA	GGACAGAGTC	AGCGCGAGGT	CTCTCAGCTC
TGAGCACATG	TTCTTTCCCC	TTCCAGGTTT	CTAGTTTTAT
GGGTAGTAGT	TTTATGATGC	CCATTTCACA	G TTCAGGCAG
G TAGAGGCAG	AGGGGAGCAT	TAAGCTGACT	TGCCCAGCGT
CACTGAGTTG	GCTACGGGCA	GCCTTCCCAA	GGGTACAGAT
GGCAAACACT	G TTCCTTATC	TCTTTCAGGT	GGCCCTGCTC
AGAGCCCATG	CTGGCGAGCA	CCTGCTGCTC	GGAGCCACCA
AGAGATCCAT	GGTGGTCAAG	GACGTGCTGC	TCCTAGGTGA
GGCGGCTGCC	TGCCCTGGCC	AGGGCTCCAG	GGAGGGTATG
CCTAGCATGG	CACTCACCCA	GGCAAGGAGA	TTCACATGGT
GGCATGCAAG	GGTGAGGGAG	ACTAGTCAGG	AGTGGCCCTG
TCCTCAGGCT	TGCATTGGAG	GGCTCCAGGA	CTCAGTTTTT
AACTGGGTAC	CCCAC TCAGA	TGCAAGGAAA	TGTGGATGCA
AGTCACCAAA	TTCCCAGCAT	AGAAGTCAGA	GCACGATCAG
GGTTATCCCT	GGAATTACCT	GTGCATCCTT	TTTTCTTTTG
ACAGAGTCTT	GCTCTGTCAC	TCAGGCTGGA	GTGCAATGAT
GTGA			

FIG. 8G



Partial Sequence of Human HNF4 Gene
(Exon 7, SEQ ID NO:48)

GCAACACTAG	TATTTTAATA	TAACAATGCT	ATGAGGGAGC
TCGATTATTT	ATCCTCATCT	TATAGATAAG	AAAAC TGAGG
CACAGAGAGG	TTAAGTAACT	TATCCAATA	TAACCAGCTA
TCAGGGGCAG	AGCCATT TAA	GCAGGGCAGT	GCAGTTCCAG
AATCTGGTCC	TTTAACCTTG	ATGCTTTGGT	GCCTATCAGG
TGACCTTTGA	ATGTCATCGA	TCTTGTGAGT	CATGTTGGTA
AATGGAGCTT	GGGTCATGTG	AAAGAGGTCC	TAGAAAGCCA
AGTTCCAAGC	TCAGCCGGAT	GACTCAAGGC	AGCTTATCTT
CTGAATCTGG	GCCTCAGCTT	CCTTACCTGT	GAAATGGGAG
TCACCATCCC	TGCAGGTCCT	CCTCCCACAG	GCACCAGCTA
TCTTGCCAAC	TTAAAAGCCA	AAACTAGAGG	AGAGGGGTCA
ACCCAAAGTG	ACTTCCCATC	CTCCCTCCCT	CCCAACCCTT
CCAGGCAATG	ACTACATTGT	CCCTCGGCAC	TGCCCCGGAGC
TGGCGGAGAT	GAGCCGGGTG	TCCATACGCA	TCCTTGACGA
GCTGGTGCTG	CCCTTCCAGG	AGCTGCAGAT	CGATGACAAT
GAGTATGCCT	ACCTCAAAGC	CATCATCTTC	TTTGACCCAG
GTACAGTGCA	CACCTCCTAA	GCCATCCCTG	ACTCTCTCTC
CAGAACGCTC	TGCCAGACTT	CTCCTATTGG	GTTCTGTACA
CTGAGTTCAC	AGCCTCATCT	CATGTTAACG	ACAGCCAGGA
GAGGCCGTTT	TCATTTAACA	GATGAGGCAA	GTCAAGATTT
GAAGAGACAA	TATGGCCGGG	CGCAGTGGCT	CACACCTGTA
ATCCCATCAC	TTTGGGAGGC	TGAGGCGGGC	GGATCACCTG
AGGTCAGGGG	TCAAGATGAG	CCTGGCTAAC	ATGGAGAAAC
CCCATCTCTA	CTTAAAA		

FIG. 8H



Partial Sequence of Human HNF4 Gene

(Exon 8, SEQ ID NO:50)

GTGGCTCTGC	CAACAACCTGG	CTGTGCGACC	CAGGACAAGT
CCTATCTTTG	CACTGTGTCT	GGGTTTCCCC	GTGTGTAAGA
TGAGGCGGTT	GCTAGGTGCT	TATTGGATGC	ATTCCTCAAG
TCCCGCCCTC	CATCTCCTAT	TCCCCTCTCT	TCTGGTTTAG
TGCTTTAGGA	AATGTGGCAG	AAATCTTTTT	CTGCCTGTGT
CTAGGAAATC	ATAATTCATG	CTGGCGTACC	CTGGTTGTTG
AGGTCCCTGA	ATCCTTGTGC	CCACACTGCT	GAAGACTCCT
TGTGTGACAC	AAGTCAGGGG	ACATCTGGGT	CTTGACTCCC
CAGATGCTCC	AGGTGGACCC	TGCTGCCCTC	CCTTGCCCAC
CCTCTTCCAT	TGTAGATGCC	AAGGGGCTGA	GCGATCCAGG
GAAGATCAAG	CGGCTGCGTT	CCCAGGTGCA	GGTGAGCTTG
GAGGACTACA	TCAACGACCG	CCAGTATGAC	TCGCGTGGCC
GCTTTGGAGA	GCTGCTGCTG	CTGCTGCCCA	CCTTGACAGAG
CATCACGTGG	CAGATGATCG	AGCAGATCCA	GTTTCATCAAG
CTCTTCGGCA	TGGCCAAGAT	TGACAACCTG	TTGGAGGAGA
TGCTGCTGGG	AGGTCCGTGC	CAAGCCCAGG	AGGGGCGGGG
TTGGATTGGG	GACTCCCCAG	GAGACAGGCC	TCACACAGTG
AGCTCACCCC	TCAGCTCCTT	GGCTTCCCCA	CTGTGCCGCT
TTGGGCAAGT	TGCTTAACCT	GTCTGTGCCT	CAGTTTCCTC
ACCAGAAAAA	TGGGAACAAG	GCAATGGTCT	ATTTGTTTCA
GCACCGAGAA	CCTAGCACGT	GCCAGTCACT	GTTCTAAGTG
CTGGCAATTC	AGCAAAGAAC	AAGATCTTTG	CCCTCGGGGA
GGCTGTGTGT	GTGTGATAT	GTATGGATGC	GTGGATATCT
GTGTATATGC	CCGTATGTGC	GTGCATGTGT	ATATAAAGCC
TCACATTTTA	TGATTTTGA		

FIG. 8I



Partial Sequence of Human HNF4 Gene
(Exon 9, SEQ ID NO:52)

GGGACACATA	GATGCTATAA	GTAGGTCAGT	TGGCTGCAGC
AGAGATGTGG	GGGATGAGGC	TGAAAGGTGA	GGCGGGACCA
AATGGTTGAA	GGACTTGCAC	TCCAAGGAGC	TTTGAGAGCC
ATTGATTACA	TCCATTATGT	TACTATGTGA	CCAATACATT
ACTCATTAGA	ACATTTACGT	GATCTCAGAG	CTTCCTTATA
TGCACCTTGT	TCCTTTCAAC	TCACTTTTGT	TCTCTTGGTT
TTTTGGGGTC	CTCTTAACAC	CCTCATGAAG	TCTATAGATG
GGAATGGTAC	ACCCTAGTTT	ACTAACCCAG	GAATAGGTAC
CCAACAGGCA	CTGCCAATAT	TGGATGGGCT	GGTTGATTGG
CCACGCCTGA	GGAAGATGGC	GTCCCAAGGC	CTGAGGTCTG
CATCCCAGAC	TCTCCATCCT	GATCGACCTT	CTCTACCTGC
AGGGTCCCCC	AGCGATGCAC	CCCATGCCCA	CCACCCCCTG
CACCCTCACC	TGATGCAGGA	ACATATGGGA	ACCAACGTCA
TCGTTGCCAA	CACAATGCCC	ACTCACCTCA	GCAACGGACA
GATGTGTGAG	TGGCCCCGAC	CCAGGGGACA	GGCAGGTGGG
CAAACCTCTGG	GATTTTACCT	TGCAAAGGGT	GAGGATGGGG
CTTAAGACAG	GAGGCAGGAG	AAAGTGGAGT	CTAGAAGGTA
GAACCAGGAT	GCAACAGTTT	TCTGGGTTC	AGGGTAGGGA
ATAAAGGGCA	AGATTGTCCA	TTTGTTGAGG	CTGTTTATTC
AGTAAGGTGA	CTGACAGCCT	TTACTGAATG	AAGCCATTGT
TGGGATGAGG	CAATCCACTG	GATGAGGTAA	CCCATTGGGT
GAAGATGTCT	TGGGTGAGAA	TTCCATTAGT	TGACATTGTC
CATTAAGTAA	AAGTGGTCAT	TGAAGTAAGG	CTGCACAGTT
GGGTAAGGCT	ATCCATTAGA	CATTAGATGA	GACTACCCAT
TGGGTCAGGA	TGTCTGCTGG	GCTA	

FIG. 8J



Partial Sequence of Human HNF4 Gene
(Exon 10, SEQ ID NO:54)

TTTGGGAGAA	GCAGTCCAAG	TCTGCATATC	AAATAAATGA
TGGAGGAGAT	GGGTGGTAGG	ACCTTCCAGA	CCTCATAAAA
CTTAGGCTTT	ATGATCTGGG	ACTCACAGAA	GGTTGAGCAA
TAAAAGACCT	TAGGGATTAT	CTGGCTTAAT	TAATTCTCTC
ATTTTATAGA	GGAAGAAATT	AAGTCAAGGT	GGGGCAGGGT
GGGAGGGGAG	AACTTTCCCG	GGGCTCTTCA	TTTACTCCCA
CAAAGGCTGG	AATTTTGAGC	AGCCCCTGTC	TGTCTGTTTG
TCCTTCCAGC	CACCCCTGAG	ACCCACAGC	CCTCACCGCG
AGGTGGCTCA	GGGTCTGAGC	CCTATAAGCT	CCTGCCGGGA
GCCGTCGCCA	CAATCGTCAA	GCCCCTCTCT	GCCATCCCCC
AGCCGACCAT	CACCAAGCAG	GAAGTTATCT	AGCAAGCCGC
TGGGGCTTGG	GGGCTCCACT	GGCTCCCCC	AGCCCCCTAA
GAGAGCACCT	GGTGATCACG	TGGTCACGGC	AAAGGAAGAC
GTGATGCCAG	GACCAGTCCC	AGAGCAGGAA	TGGGAAGGAT
GAAGGGCCCCG	AGAACATGGC	CTAAGGCACA	TCCCCTGCA

FIG. 8K-1



Partial Sequence of Human HNF4 Gene
(Exon 10, SEQ ID NO:54)

CCCTGACGCC	CTGCTCTGAT	AACAAGACTT	TGACTTGGGG
AGACCCTCTA	CTGCCTTGGA	CAACTTTCTC	ATGTTGAAGC
CACTGCCTTC	ACCTTCACCT	TCATCCATGT	CCAACCCCCG
ACTTCATCCC	AAAGGACAGC	CGCCTGGAGA	TGACTTGAGC
CTTACTTAAA	CCCAGCTCCC	TTCTTCCCTA	GCCTGGTGCT
TCTCCTCTCC	TAGCCCCGGT	CATGGTGTCC	AGACAGAGCC
CTCTGAGGCT	GGGTCCAATT	GTGGCACTTG	GGGCACCTTG
CTCCTCCTTC	TGCTGCTGCC	CCCACCTCTG	CTGCCTCCCT
CTGCTGTCAC	CTTGCTCAGC	CATCCCGTCT	TCTCCAACAC
CACCTCTACA	GAGGCCAAGG	AGGCCTTGGA	AACGATTCCC
CCAGTCATTC	TGGGAACATG	TTGTAAGCAC	TGACTGGGAC
CAGGCACCAG	GCAGGGTCTA	GAAGGCTGTG	GTGAGGGAAG
ACGCCTTTCT	CCTCCAACCC	AAC	

FIG. 8K-2

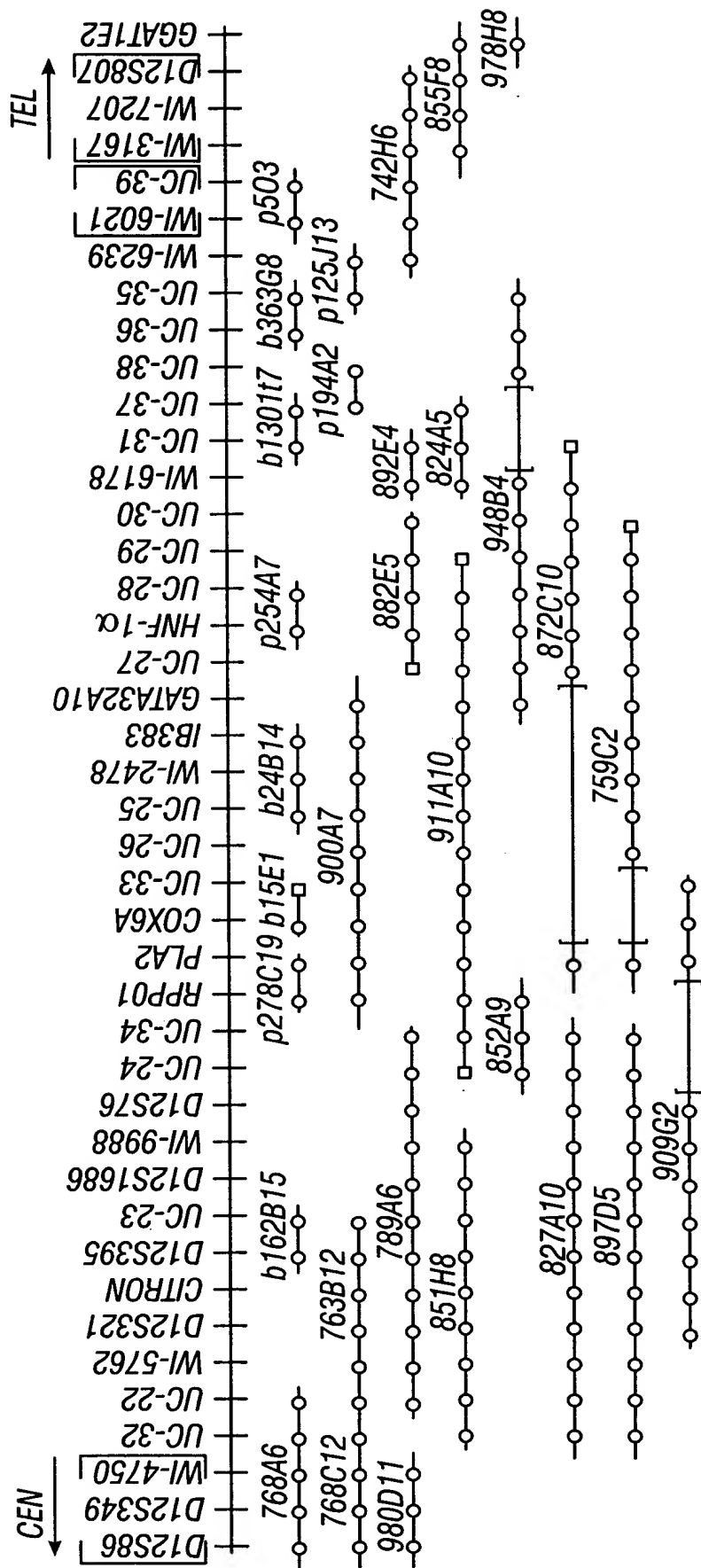


FIG. 9

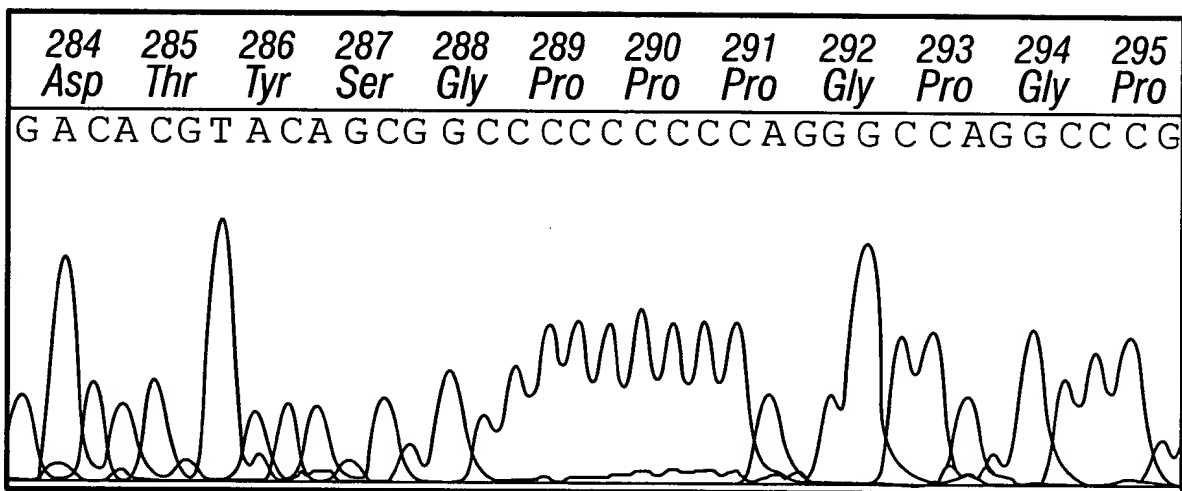
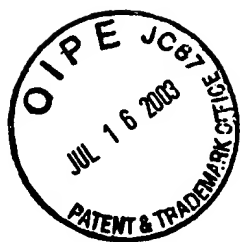


FIG. 10A

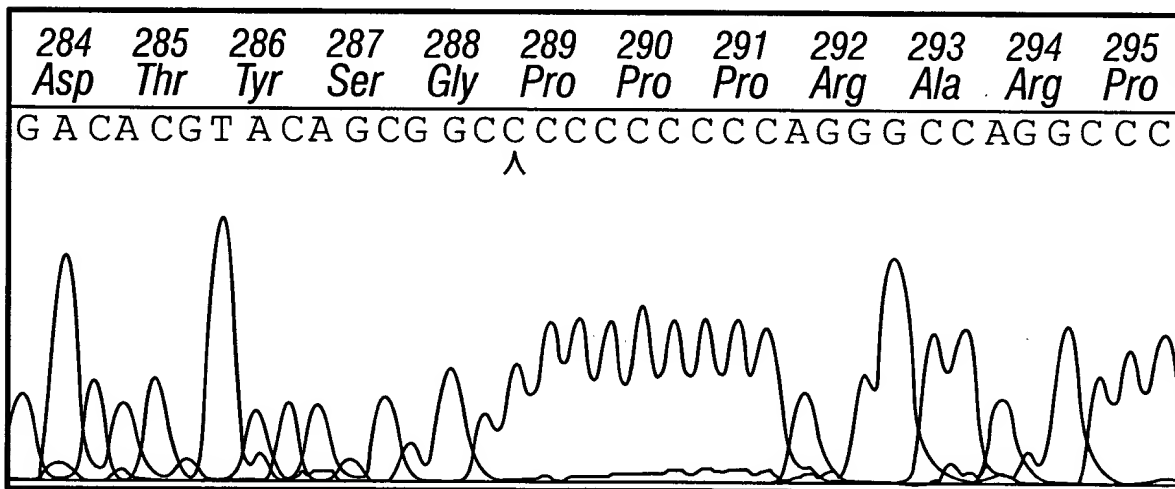
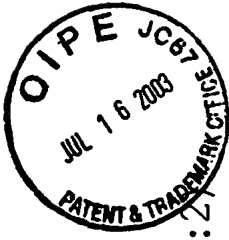


FIG. 10B



Translation of human HNF1a Sequence (cDNA=SEQ ID NO:1 and protein=SEQ ID NO:2)

1

20

Met Val Ser Lys Leu Ser Gln Leu Gl
GGCCCTGTGGCAGCCGAGCC ATG GTT TCT AAA CTG AGC CAG CTG CAG

30

50

Ala Leu Ile Gln Ala Leu Gly Glu Pro Gly Pro Tyr Leu Leu Al
GCA CTG ATC CAG GCA CTG GGT GAG CCG GGG CCC TAC CTC CTG GC

60

80

Gly Glu Leu Ala Glu Leu Pro Asn Gly Leu Gly Glu Thr Arg Gl
--- GAG CTG GCT GAG CTG CCC AAT GGG CTG GGG GAG ACT CGG GG

90

Exon 1 | 110 Exon 2

Ile Leu Lys Glu Leu Glu Asn Leu Ser Pro Glu Glu Ala Ala Hi
ATC CTC AAA GAG CTG GAG AAC CTC AGC CCT GAG GAG GCC CA

120

FIG. 11A-1



10

Thr Glu Leu Leu Ala Ala Leu Leu Glu Ser Gly Leu Ser Lys Glu
ACG GAG CTC CTG GCG GCC CTG CTC GAG TCA GGG CTG AGC AAA GAG

40

Gly Glu Gly Pro Leu Asp Lys Gly Glu Ser Cys Gly Gly Arg
GGA GAA GGC CCC CTG GAC GAC AAG GGG GAG TCC TGC GGC GGT CGA

70

Ser Glu Asp Glu Thr Asp Asp Asp Gly Glu Asp Phe Thr Pro Pro
TCC GAG GAC GAG ACG GAC GAC GAT GGG GAA GAC TTC ACG CCA CCC

100

Gln Lys Ala Val Val Glu Thr Leu Leu Glⁿ Glu Asp Pro Trp Arg
CAG AAA GCC GTG GTG GAG ACC CTT CTG CA^G GAG GAC CCG TGG CGT

130 Gln(Hinek-missense)

140

FIG. 11A-2



Val Ala Lys Met Val Lys Lys Ser Tyr Leu Gln Gln His Asn Ile Pro
GTG GCG AAG ATG GTC AAG TCC TAC TAC CAG CAG CAC AAC ATC CCA

150

Exon 2

170 Ser Gln His Leu Asn Lys Gly Thr Pro Met Lys Thr Gln Lys Arg
TCC CAA CAC CTC AAC AAG GGC ACT CCC ATG AAG ACG CAG AAG CGG

Exon 3 180

200 G|ln Gln Phe Thr His Ala Gly Gln Gly Gly Leu Ile Glu Glu Pro
C|AG CAG TTC ACC CAT GCA GGC CAG GGA GGG CTG ATT GAA GAG CCC

210

230 Lys Trp Gly Pro Ala Ser Gln Gln Ile Leu Phe Gln Ala Tyr Glu
AAG TGG GGC CCA GCA TCC CAG CAG ATC CTG TTC CAG GCC TAT GAG

FIG. 11B-1



140

Gln Arg Glu Val Val Asp Thr Thr Gly Leu Asn Gln Ser His Leu
CAG CGG GAG GTG GTC GAT ACC ACT GGC CTC AAC CAG TCC CAC CTG

A

160

Ala Ala Leu Tyr Thr Trp Tyr Val Arg Lys Gln Arg Glu Val Ala
GCC GCC CTG TAC ACC ACC TGG TAC GTC CGC AAG CAG CGA GAG GTG GCG

190

Thr Gly Asp Glu Leu Pro Thr Lys Lys Gly Arg Arg Asn Arg Phe
ACA GGT GAT GAG CTA CCA ACC AAG AAG GGG CGG AGG AAC CGT TTC

220

Arg Gln Lys Asn Pro Ser Lys Glu Glu Arg Glu Thr Leu Val Glu
AGG CAG AAG AAC CCT AGC AAG GAG GAG CGA GAG ACG CTA GTG GAG

FIG. 11B-2



Exon 3		Exon 4	
260	Glu Cys Asn Arg	g Ala Glu Cys Ile Gln Arg Gly Val Ser Pro Ser	
	GAG TGC AAT AG	G GCG GAA TGC ATC CAG AGA GGG GTG TTC CCA TCA	
270			
290	Tyr Asn Trp Phe Ala Asn Arg Arg Lys Glu Glu Ala Phe Arg His		
	TAC AAC TGG TTT GCC AAC CGG CGC AAA GAA GAA GCC TTC CGG CAC		
CCCC (Donoghue - C insertion)			
	Pro Gly Pro Ala Leu Pro Ala His Ser Ser Pro Gly Leu Pro Pro		
	CCG GGA CCT GCG CTG CCC GCT CAC AGC TCC CCT GGC CTG CCT CCA		
330			
350	Pro Ala Thr Ser Glu Thr Ala Glu Val Pro Ser Ser Ser Gly Gly		
	CCT GCG ACC AGT GAG ACT GCA GAA GTA CCC TCA AGC AGC GGC GGT		

FIG. 11C-1



250

Gln Ala Gln Gly Leu Gly Ser Asn Leu Val Thr Glu Val Arg Val
CAG GCA CAG GGG CTG GGC TCC AAC CTC GTC ACG GAG GTG CGT GTC

280

Lys Leu Ala Met Asp Thr Tyr Ser Gly Pro Pro Gly Pro Gly
AAG CTG GCC ATG GAC ACG TAC AGC GGG CCC CCC CCA GGG CCA GGC

		Exon 4		320	Exon 5										
Pro	Ala	Leu	Ser	Pro	Ser	Lys	Val	His	Gly	Val	Arg	Gly	Gln		
CCT	GCC	CTC	TCC	CCC	AGT	AAG	GTC	CAC	G	GT	GTG	CGC	TNT	GGA	CAG

340

Pro Leu Val Thr Val Ser Thr Pro Leu His Gln Val Ser Pro Thr
CCC TTA GTG ACA GTG TCT ACA CCC CTC CAC CAA GTG TCC CCC ACG

FIG. 11C-2



(Pratt - mutation splice acceptor site Exon 6, AG--> GG)
Exon 5
360

Gly Leu Glu Pro Ser His Ser Leu Ser Thr Glu Ala Lys Leu
GGC CTG GAG CCC AGC CAC AGC CTG CTG AGT ACA GAA GCC AAG CTG

C-- (Newton - CT deletion)

Ala Leu His Ser Leu Glu Gln Thr Ser Pro Gly Leu Asn Gln Gln
GCA CTG CAC AGC TTG GAG CAG ACA TCC CCA GGC CTC AAC CAG CAG

420

Exon 6 | Exon 7 440

Gly Pro Gly Glu Pro Ala Ser Leu Gly Pro Thr Phe Thr Asn Thr
GGG CCT GGT GAG CCT GCC TCC TCC CTG GGT CCT ACG TTC ACC AAC ACA

450

470
Ser Val Pro Val Ile Asn Ser Met Gly Ser Ser Leu Thr Thr Leu
AGT GTG CCG GTC ATC AAC AGC ATG GGC AGC AGC CTG ACC ACC CTG

FIG. 11D-1



370 Exon 6

Val Ser Ala Ala Gly Gly Pro Leu Pro Pro Val Ser Thr Leu Thr
GTC TCA GCA GCT GGG GGC CCC CTC CCC CCT GTC AGC ACC CTG ACA

Pro Gln Asn Leu Ile Met Ala Ser Leu Pro Gly Val Met Thr Ile
CCC CAG AAC CTC ATC ATG GCC TCA CTT CCT GGG GTC ATG ACC ATC

430

Gly Ala Ser Thr Leu Val Ile Ile Gly Leu Ala Ser Thr Gln Ala Gln
GGT GCC TCC ACC CTG GTC ATC ATC G|GC CTG GCC TCC ACG CAG GCA CAG

460

Gln Pro Val Gln Phe Ser Gln Pro Leu His Pro Ser Tyr Gln Gln
CAG CCC GTC CAG TTC TCC CAG CCG CCG CTG CAC CCC TCC TAC CAG CAG

FIG. 11D-2



480
Exon 7 500 | Exon 8
Pro Leu Met Pro Pro Val Gln Ser His Val Thr Gln Ser Pro Phe
CCG CTC ATG CCA CCT GTG CAG AGC CAT GTG ACC CAG AGC CCC TTC

510

530
His Lys Pro Glu Val Ala Gln Tyr Thr His Thr Gly Leu Leu Pro
CAC AAG CCC GAG GTG GCC CAG TAC ACC CAC ACG GGC CTC CCG

540 | Exon 9

560
Ser Leu Thr Pro Thr Lys Gln | Val Phe Thr Ser Asp Thr Glu Ala
AGC CTC ACG CCC ACC AAG CAG | GTC TTC ACC TCA GAC ACT GAG GCC

570

Exon 9 | 590 Exon 10
Leu His Val Pro Ser Gln Asp Pro Ala Gly Ile Gln His Leu Gln
CTC CAC GTC CCC AGC CAG GAC CCT GCC GGC ATC CAG CAC CTG CAG

FIG. 11E-1



490

Met Ala Thr Met Ala Gln Leu Gln Ser Pro His A|la Leu Tyr Ser
ATG GCC ACC ATG GCT CAG CTG CAG AGC CCC CAC G|CC CTC TAC AGC

A

520

Gln Thr Met Leu Ile Thr Asp Thr Thr Asn Leu Ser Ala Leu Ala
CAG ACT ATG CTC ATC ACC GAC ACC ACC AAC CTG AGC GCC CTG GCC

550

Ser Ser Glu Ser Gly Leu His Thr Pro Ala Ser Gln Ala Thr Thr
TCC AGT GAG TCC GGG CTT CAC ACG CCG GCA TCT CAG GCC ACC ACC

580

Pro Ala His Arg Leu Ser Ala Ser Pro Thr| Val Ser Ser Ser Ser
CCG GCC CAC CGG CTC AGC GCC AGC CCC ACA| GTG TCC TCC AGC AGC

FIG. 11E-2



620
Leu Val Leu Tyr Gln Ser Ser Asp Ser Ser Asn Gly Gln Ser His
CTG GTG CTG TAC CAG AGC TCA GAC TCC AGC AAT GGC CAG AGC CAC

600

630 631

CAG ATG GCC TCT TCC TCC CAG TAACCACGGCACCTGGGCCCTGGGGCCTGTAC
AGCAACCGTGGCCCTTCCTGGACAGCTGTGCCCTCGCTCCCCACTCTGCTCTGATGCATCA
GTCGTGGAGAGCTAGGAGCAAAGCCCTGTTTCATGGCAGATGTAGGAGGACTGTCGCTGCT
CAGCCTGGGCCCTATGGAGAGCCCTGGGACCGCTACACCACTCTGGCAGCCACACTTCTCA
CTTGTTCTGTACCAATGTACCCACCGGCCACTCCTTCCTGCCCCCACTCCTTCCAGCT
GGCTACTCTGTGCCAGAGCCTGGGGCTCTAACTGCCCTGAGCCCAGGGAGGCCGAAGCTAA
CCCATGACCTCCAGCTTTCCTGTATTTCTTCCCAAGAGCATGATGCCCTGTAGGCCAGCC

FIG. 11F-1



610

Leu Leu Pro Ser Asn His Ser Val Ile Glu Thr Phe Ile Ser Thr
CTG CTG CCA TCC AAC CAC AGC GTC ATC GAG ACC TTC ATC TCC ACC

CTGCCCTGCTTGGGGGTGATGAGGCGCAGCCAGCCCTGCCCTGGAGGACCTGAGCCTGCGG
AGAAAGGAGGGCTCTGAGGCGCCCCAACCCGTGGAGGCTGCTCGGGGTGCACAGGAGGGG
TTCGTGGGATACAGTCTTCTTACTTGGAACTGAAGGGCGGCCCTATGACTTGGGCACCCC
AGGACACAGGCCTGTGTAGCTGTGACCTGTGAGCTCTGAGAGGCCCTGGATCAGCGTGGC
TAGTGACCCACATGCCATTGTACTGACCCCATCACCTACTCACACAGGCATTTCCTGGGT
ACAGGGAAGCAGGCAGGGCTCTCCTGGTCTTCCCATCCCCAGCGATTCCCTCTCCCAGGC
CTGGCCTCCTGCCTCTACTGGGAAGGCTACTTCGGGGCTGGGAAGTCGTCTTACTCCTGT

FIG. 11F-2



GGGAGCCTCGCAACCCGTGCCAAGTCCAGGTCCTGGTGGGCAGCTCCTCTGTCTCGAGC
CCGAGCAGCTGAGCAGGGCCGGGGAACCTGGCCAAGCTGAGGTGCCCAGGAGAAGAAAGAG
CCTGGCTGGCTGAGGGCAGTTTCGCAGCCACCCTGAGGAGTCTGAGGTCCTGAGCACTGCC
TGCTGAGAACCTGGCCTTCAGTGTAACCGCGTCTACCCCTGGGATTCAGGAAAGGCCTGGG
TTTAGTAAAGTCAAGGAGAAATGCGGTGG

FIG. 11G-1



GCCCTGCAGACCCCTGCCCTTGTTTGGGGCAGGAGTAGCTGAGCTCACAAGGCAGCAAGGC
GTGACCCAGGGCACAGGAGCTACCTGTGTGGACAGGACTAACACTCAGAAGCCTGGGTG
AGGAGGGACAAAGGAGCCTGTGAACCCAGGACAAAGCATGGTCCCACATCCCCTGGGCCCTGC
GTGACCCGGCACCCCTGCAGCTTGTAGCCAGCCGGGGCGAGTGGCACGTTATTTAACCT

FIG. 11G-2

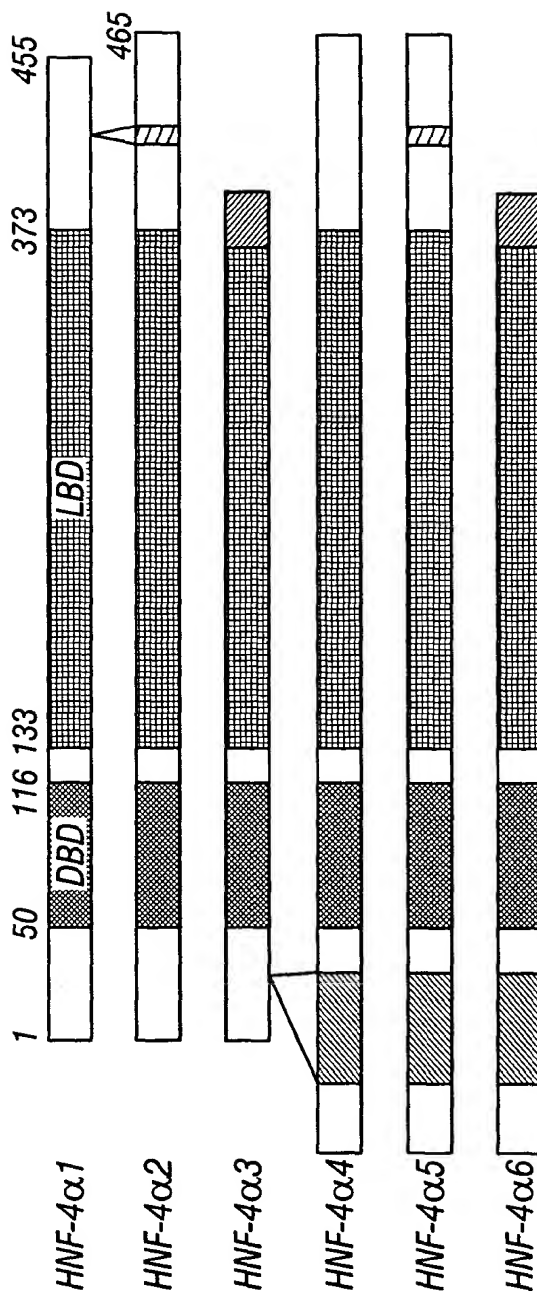
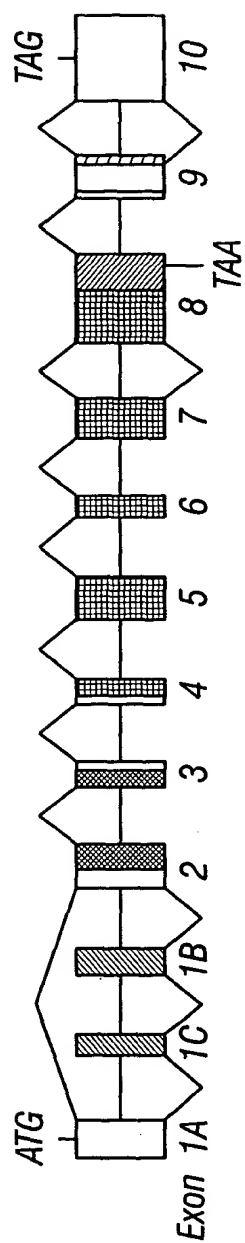


FIG. 12

human TGGGGCCTGGGAATTAGGTTTCTAATACTGTGGGCCAATGGGGCAGCCCTTAT
 mouse TGGGCTTGGGTCTTAGGTTTCTAGTTCAAGCCGACCCAGGACAGCCTTAT

618

HNF-6

human CTC TGCAAAAGCATTGAGGGTAGAAGTCAATGATTTGGGAAGTTATTGAA
 mouse CTC ---AAA---TTGAGGATAGAAGTCAATGATCTGGACGTGATTGGC

668

human TTAGGGGATCTCGAGGTAGGCT-GTCAGTGCCCTGATAGTATCAGTTAGA
 mouse TTAGGGCTTCAATAGTGGTAGGCTTGCAGTGTCATAAATGTCAGCTGGG

717

human ATGCTGACTTGGGGTGACAATGGCTTGAGGGGTGGGTGAGTCAAGGG-
 mouse TTGTCCA CCTTG--GTGA----GACTTGG--GGCTGCTGAGCAAGGGG

766

FIG. 13A

human TCAATGAGTGCCCGTAGTCAATGCGCTGCCCTTGTAACAATTGATAACT
mouse TCCAAACCAATGCCAGTCTGTTGGTGCCCTGCCCTTGGAAGATTGGTAAGT

816

human GACATCGGTGAGTTAGGGCCC-----CAGCAGTTGTAATTAGCAC
mouse GACTATTAAATGAGCGGAGGTGGGGGGGGGCAACAGTTGTAATTAGCAC

857

AP - 1 HNF - 3

human CCCGGGTGTCAGCCAGAAACCAACAAACAGCCAAATCCCTGCAGCCCCGC
mouse CCCAGGTGTCAGTCAGAAACCAACAAACAGCCAAATCCCTCGTGGCTCCAC

907

HNF - 1 α

human CCAGCCTATCCAACCGCGGGGAGCCGATTAAACCATTAACCCACCCCTC
mouse CCAGCCTACCCAGCAACGGGGG--TGATTAAACCATTAACCTACCCCTC

957

NF - 1

human CCCGGCAGAGCCTCCACCCCTTCAACAGAGGCTAGGCCCAAGACTCCAGCA
mouse CCQA-CAGAGCCTCCACCC-[CTGCAGAGGCTAGGCCAGGAGGCCAGGCT

1007

FIG. 13B

*

human GATCTTCCAGAGGACGGTTTGAAAG-----GAAGGCAGAGAGGGCAC-TG 1052
mouse GAGTCTCCAGAGGACAGTTTGAAAGAGAGGAAGGCAGAGAAAGGACCTG

human GGAGAGGCAGTGGAGGGCGGAG--GGCGGGGGCC-----TTCGG 1091
mouse GGAGAGGCAGGAGGAGGCGGGACGGGGGGCTGGGCTCAGCCQAG

human GG---TGGGCG---CCCAGG---GTAGGCAGGTGGCCGGCGGTGGA 1130
mouse GGGCTTGGGTGGCATCCTGGGCCGGCCAGGACAGCGGGCTAAAGCGGTGGG

human GCGAGGGAGAAATGCGACTCTCCAAACCCTCGTCGAATGGAATG 1176
mouse TA-GGGAGAAATGCGACTCTCTAAACCCTTCCTCGGCAATGGATATG

FIG. 13C



Normal Allele

<u>125</u>	<u>126</u>	<u>127</u>	<u>128</u>	<u>129</u>
<u>G C G G</u>	<u>G A C C</u>	<u>G G A T</u>	<u>C A G C</u>	<u>A</u>
<i>Arg</i>	<i>Asp</i>	<i>Arg</i>	<i>Ile</i>	<i>Ser</i>

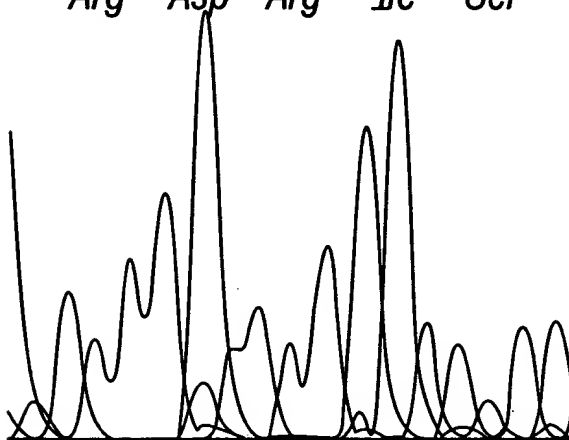


FIG. 14A

Mutant Allele

<u>G C G G</u>	<u>G A C T</u>	<u>G G A T</u>	<u>C A G C</u>	<u>A</u>
		<i>Trp</i>		

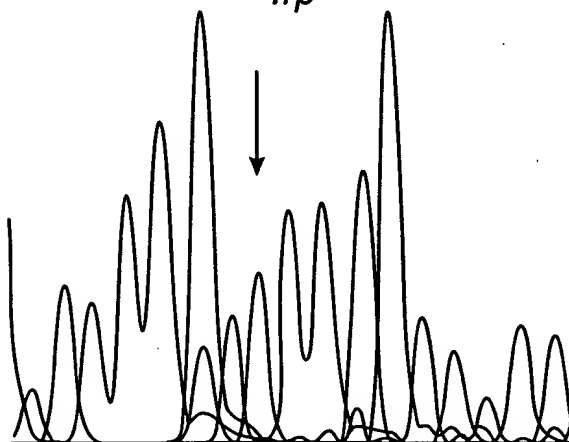
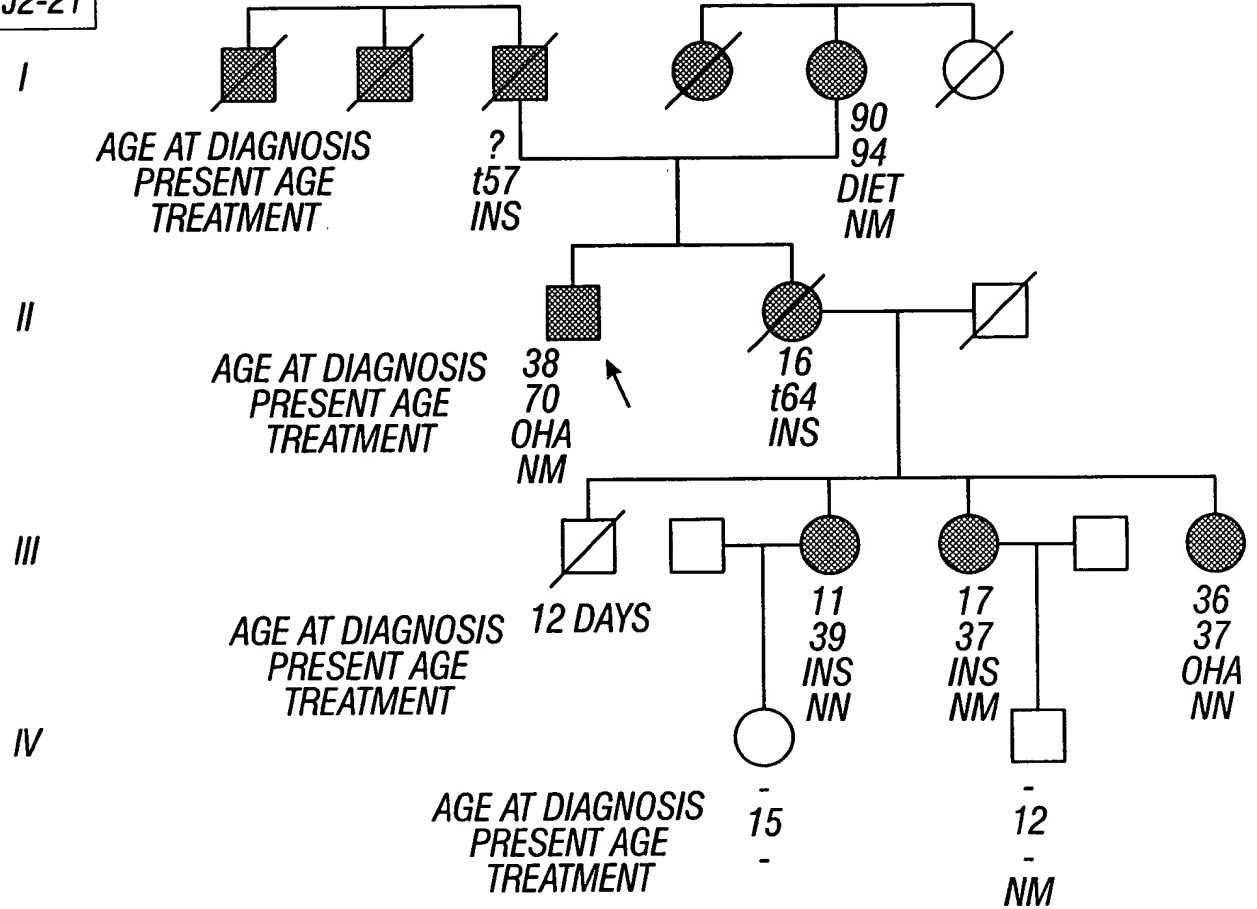


FIG. 14B

J2-21



J2-96

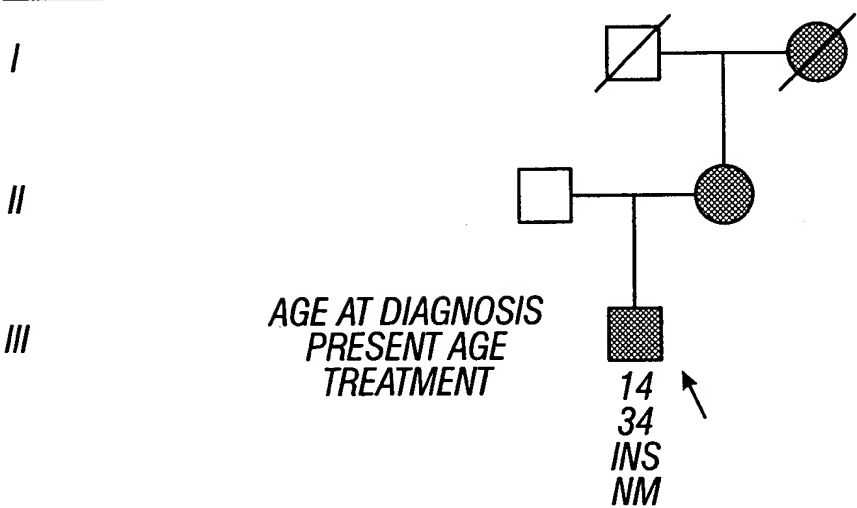


FIG. 15



I
AGE AT DIAGNOSIS
PRESENT AGE
PRESENT THERAPY
COMPLICATIONS

D20S96
D20S43
D20S169
HNF-4 α
D20S89
D20S119
D20S424

44 YEARS
64 YEARS
INSULIN
R,M,N

8	2
6	6
3	1
M	N
1	6
6	1
5	15

62 YEARS
-
-
-

8	4
1	6
3	3
N	N
9	10
1	8
8	10

II
AGE AT DIAGNOSIS
PRESENT AGE
PRESENT THERAPY
COMPLICATIONS

D20S96
D20S43
D20S169
HNF-4 α
D20S89
D20S119
D20S424

28 YEARS
47 YEARS
OHA
-

-
41 YEARS
-
-

18 YEARS
37 YEARS
INSULIN
R

25 YEARS
33 YEARS
OHA
-

1	
6	
3	
N	
3	
2	
6	

8	4
6	6
3	3
M	N
1	10
6	8
5	10

8	8
6	6
3	3
N	N
5	7
4	4
14	11

8	4
6	6
3	3
M	N
1	10
6	8
5	10

8	8
6	1
3	3
M	N
1	9
6	1
5	8

FIG. 16-1



III

AGE AT DIAGNOSIS	17 YEARS	14 YEARS
PRESENT AGE	18 YEARS	14 YEARS
PRESENT THERAPY	OHA	-
COMPLICATIONS	-	-

D20S96	8 1	8 8
D20S43	6 6	6 6
D20S169	3 3	3 3
HNF-4 α	M N	M N
D20S89	1 3	1 7
D20S119	6 2	6 4
D20S424	5 6	5 11

FIG. 16-2

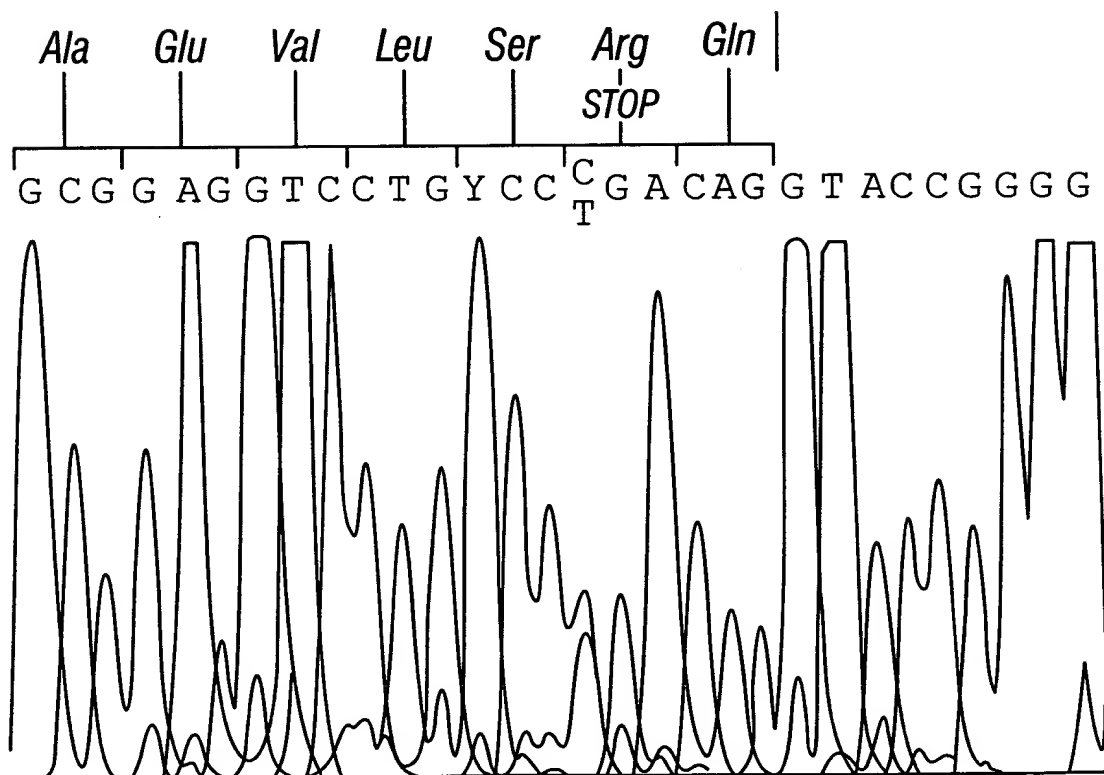
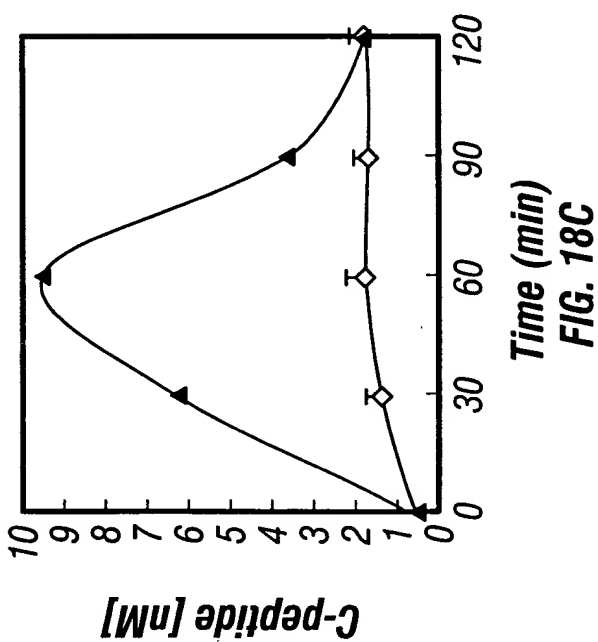
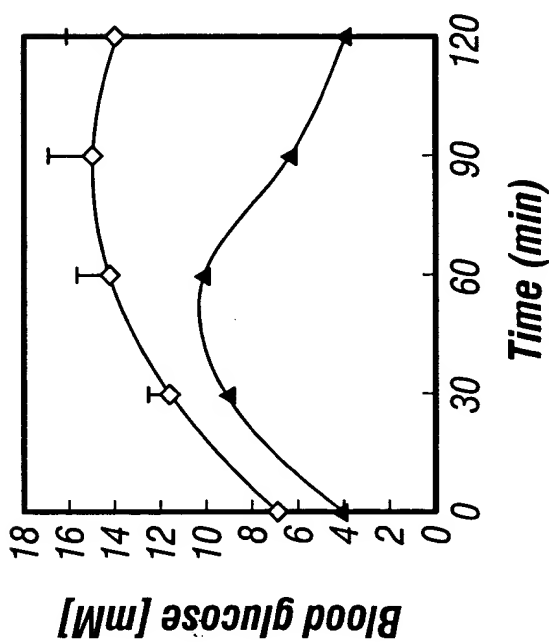
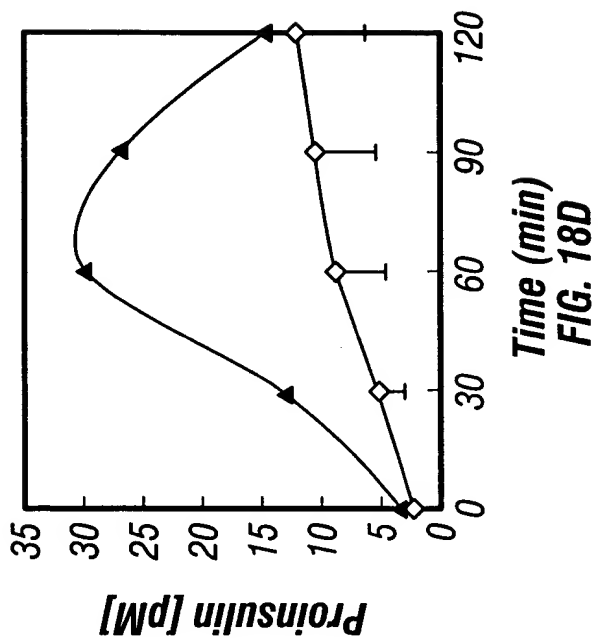
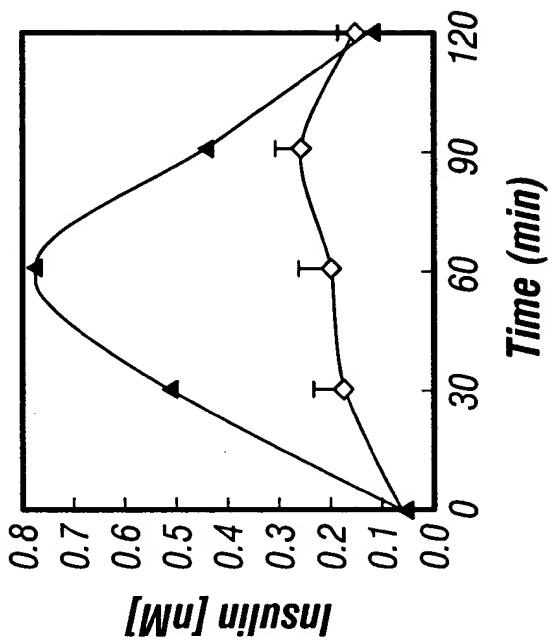
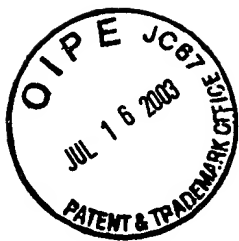


FIG. 17





- NONDIABETIC HNF-4 α MUTATION NEGATIVE $n=7$
- NONDIABETIC HNF-4 α MUTATION POSITIVE $n=7$
- ▲ DIABETIC HNF-4 α MUTATION NEGATIVE $n=7$

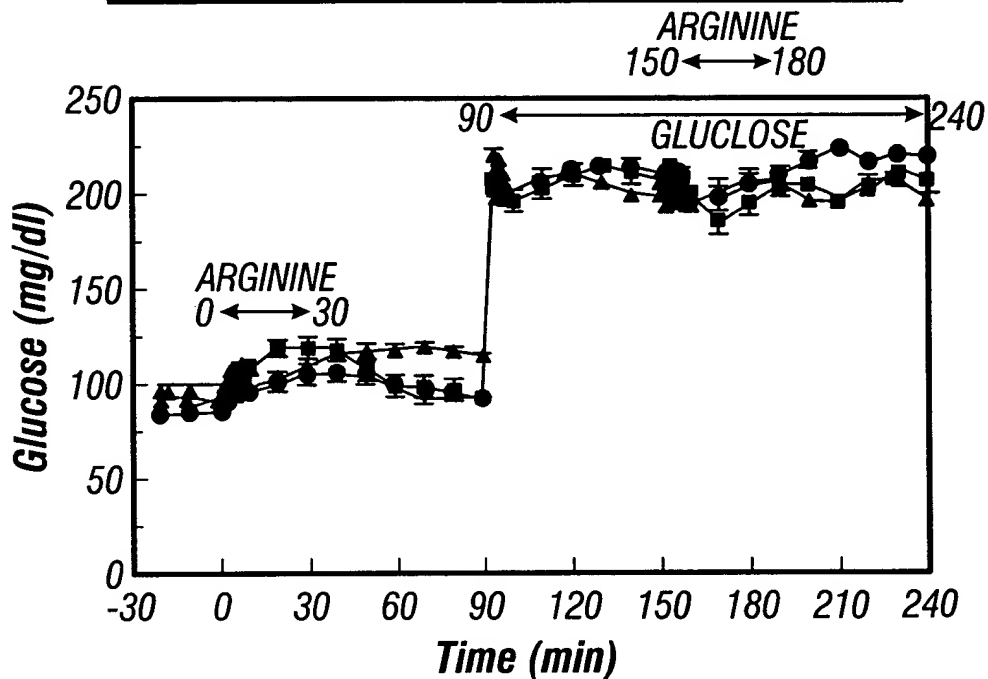


FIG. 19A

- NONDIABETIC HNF-4 α MUTATION NEGATIVE $n=7$
- NONDIABETIC HNF-4 α MUTATION POSITIVE $n=7$
- ▲ DIABETIC HNF-4 α MUTATION NEGATIVE $n=7$

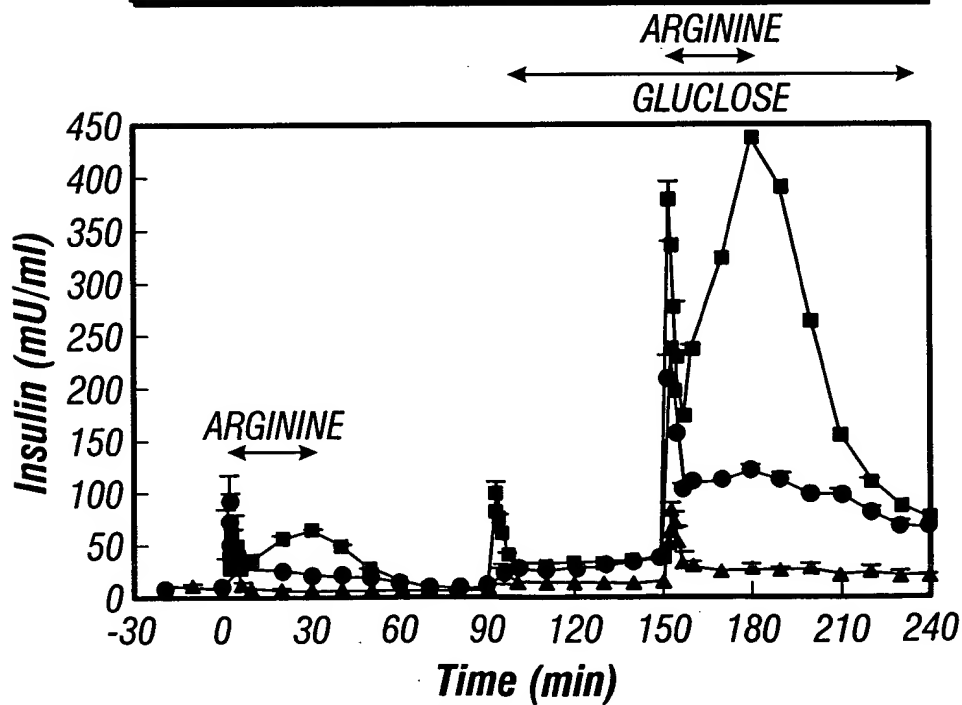


FIG. 19B



- NONDIABETIC HNF-4 α MUTATION NEGATIVE $n=7$
- NONDIABETIC HNF-4 α MUTATION POSITIVE $n=7$
- ▲ DIABETIC HNF-4 α MUTATION POSITIVE $n=4$

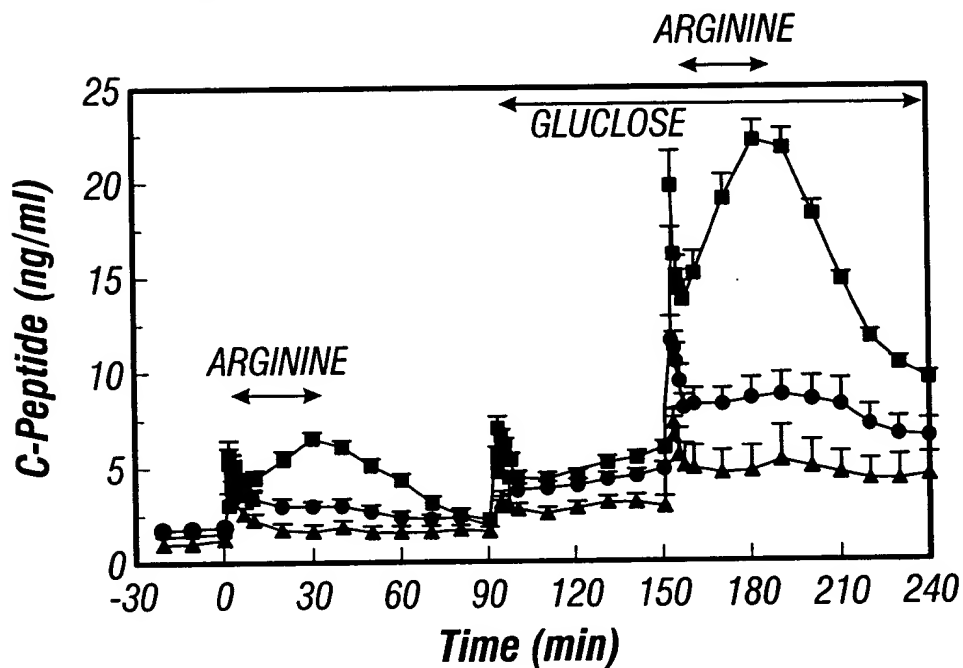


FIG. 19C

- NONDIABETIC HNF-4 α MUTATION NEGATIVE $n=7$
- NONDIABETIC HNF-4 α MUTATION POSITIVE $n=7$
- ▲ DIABETIC HNF-4 α MUTATION POSITIVE $n=4$

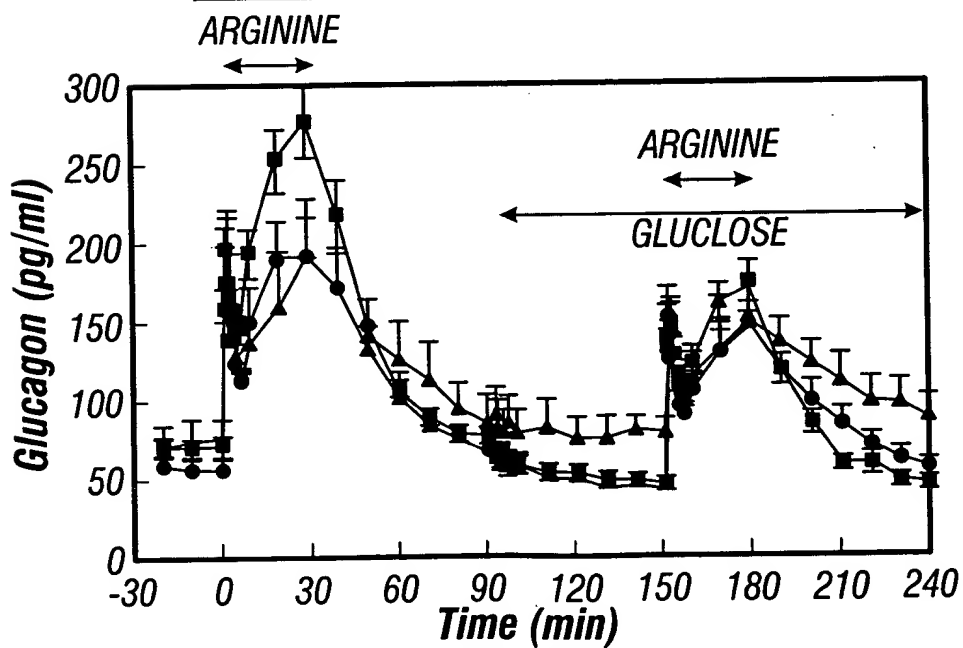


FIG. 19D



- NONDIABETIC HNF-4 α MUTATION NEGATIVE $n=7$
- NONDIABETIC HNF-4 α MUTATION POSITIVE $n=7$
- ▲ DIABETIC HNF-4 α MUTATION POSITIVE $n=4$

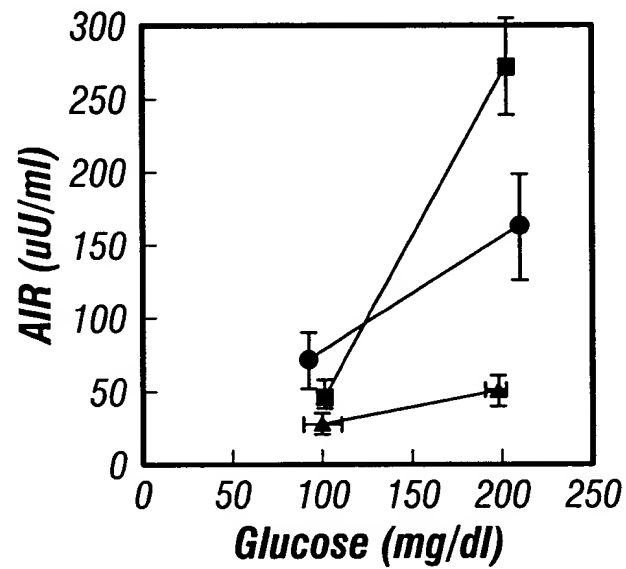


FIG. 20A

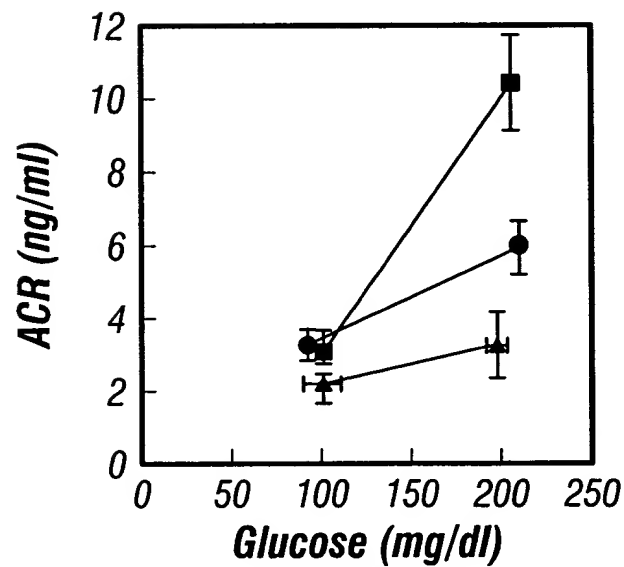


FIG. 20B

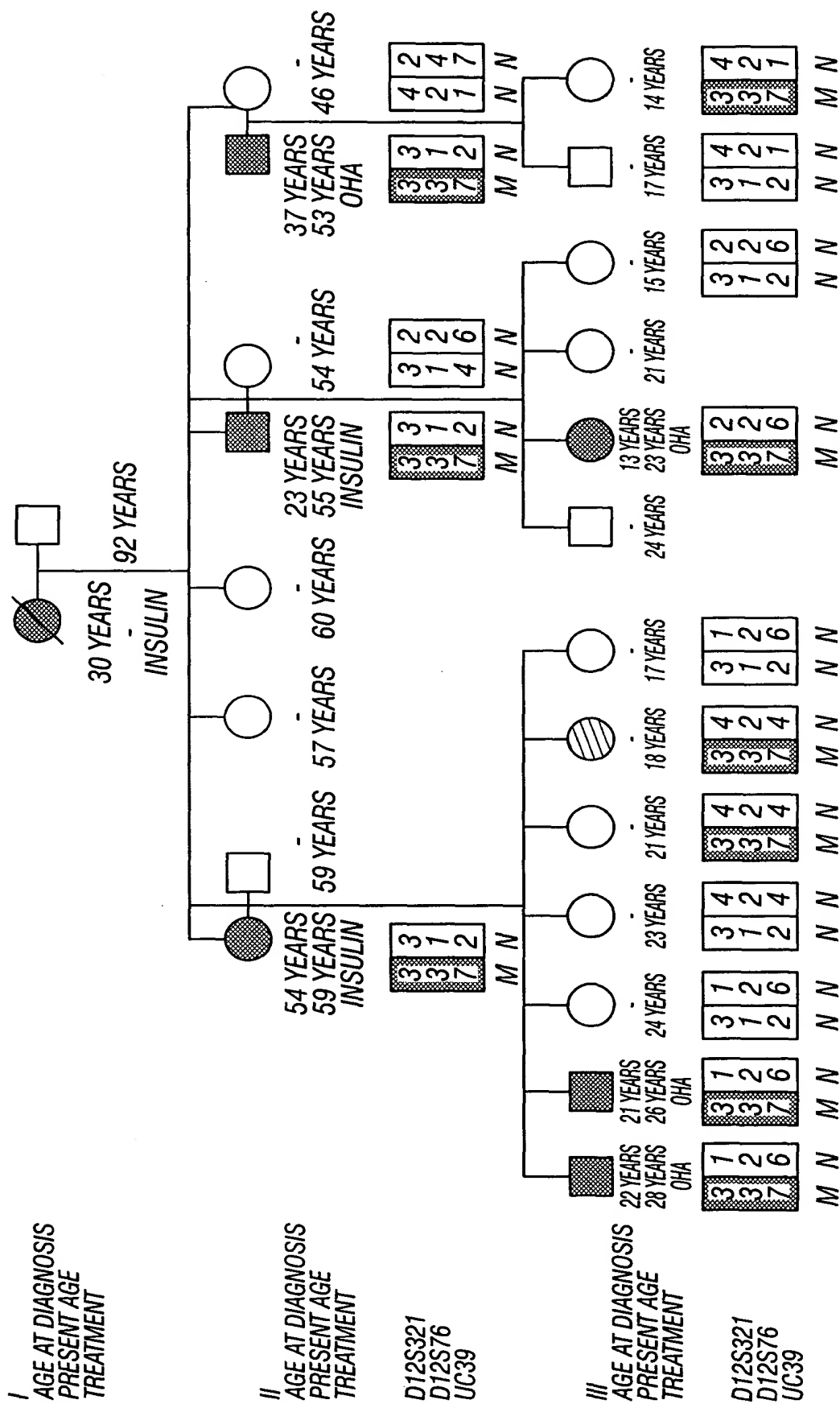


FIG. 21

human
 rat
 mouse
 chicken
 frog

-192

T T T C G G G - G G T G G G A C - C C A A C G C T G C T C T - C C T G A T G G C C T C - - C C T G - G C T C C C A G C A
 T C T T G G G C A G T G G G A C - C - A G C G C T G C T C - - C C A G A - G G C C T C - - C - T G - G C T C C T G G T G
 T C C T G G A G A G T G G G A C - C C A G C G C C G C A C - - C C A G A - G G C C T C - - C - T G - G C T C C T G C T G
 A A G T A A G C C T T G T T T T - T C C A C A C T C A T T C - T C C C A G G T T T T C - - T T T G - G A T A G G C T T A
 T C A C A G C T A T T A G C T C A T C G C T G C C A A A T T G C C C C T T T A C C T A G G C T G T G T C A C T T T C A

human
 rat
 mouse
 chicken
 frog

-134

C C T T C C A T C C C A G C T G C T C A G G G C C C C T C A C C T G - C G C C T C C C C A C C C T C C C C T C T G C -
 C C T - C T C T C C C T G C - G C C C C T G G T T C C C G - - C T C - C A C C T C C C C A C C C G C C C T T C T G C -
 C C T - C T A G C C C T G C - G C C C C T G G C C C C T - - - C T C - C A C C T C C C C A C C C T C C C T T C T G C -
 C T T T - - - T C C A T G C T G A G G A G G G C T A T C C C C T T - C A T T T T G C C T C T C C C G C T T C C C T C -
 C C T T C T C A T T C T T A C T T T T A C A T T C T T C C T T G A T A T T T T G C T T T T T C A A C T T T T G G A A

human
 rat
 mouse
 chicken
 frog

-81

- C C A C T C C C C A - T C G C A G G C C A T A G C T C C C T G T C C - - - C T C T C - C G C T G C C A T G A G G C C T
 - T C A C T C C C A A T T G C A A G C C A T G G C T C C C G T C C G - G T C C C T C T C G C T G C T G T G A G G C C T
 - T C A C T C C C A A T T G C A G G C C A T G A C T C C - G G T C C G C G T C C T C T C A C C C C A T G A G G C C T
 - C C T C T C C C C C T - - - - - C C C C C T G C T T T C - T C T C C C C T G C A C T T T G T G A A C T
 A T T T C T T T C T C T C T T C T A C C C C T C T C T A T T C C T C T G C A C T C C C C C C T C T C T A A C T C A T

FIG. 22A



C HNF-4 α

human
rat
mouse
chicken
frog

GCACCTTTCAGGGCTGAAGTCCAAAGTTCAGTCCCTTCGCTAAGCACACGGATAAATATG
GCACCTTTCAGGGCTGAAGTCCAAAGTTCAGTCCCTTCGCTAAGCACACGGATAAATATG
GCACCTTTCAGGGCTGAAGTCCAAAGTTCAGTCCCTTCGCTAAGCACACGGATAAATATG
GCACCTTTCAGGGCTGAAGTCCAAAGTTCAGTCCCTTCGCTAAGCACACGGATAAATATG
GCACCTTTCAGGGCTGAAGTCCAAAGTTCAGTCCCTTCGCTAAGCACACGGATAAATATG
GCACCTTTCAGGGCTGAAGTCCAAAGTTCAGTCCCTTCGCTAAGCACACGGATAAATATG

-21

*

human
rat
mouse
chicken
frog

AACCTTGGAGAAATTTCCCCAGCTCCAATGTAAACAGAAACA-GGCAGGGGCCCTGAT-TCA
AACCTTGGAGAAATTTCCCCAGCTCCAATGTAAACAGAGCA-GCAGGGGGCCCTGAT-TCA
AACCTTGGAGAAATTTCCCCAGCTCCAATGTAAACAGAGCA-GGCAGGGGCCCTGAT-TCA
AACCTTGGAGAAATTTCCCCAGCTCCAATGTAAACAGAGCA-GGCAGGGGCCCTGAT-TCA
AACCTTGGAGAAATTTCCCCAGCTCCAATGTAAACAGAGCA-GGCAGGGGCCCTGAT-TCA
AACCTTGGAGAAATTTCCCCAGCTCCAATGTAAACAGAGCA-GGCAGGGGCCCTGAT-TCA

+37

human
rat
mouse
chicken
frog

CGGGCCGCTGGGGCCAGG-GTTGGGGGTTGGGGTGCCACAGGGCTTGCTAGTGGGGT
CTAGCCGCTGGGGCCAGG-GTTGGGGGTTGGGGTGCCACAGGGCTTGACTAGTGGGAT
CTGGCCGCTGGGGCCAGG-GTTGGGGGTTGGGGTGCCACAGAGCTTGACTAGTGGGAT
GCACCTGGCTCAGGACAGTCTGGGGGTTCTGAAGTGGCT-CA-ATTCTGTATTTGTTT
TGCTCTCAGAGAAAGCCTGTCCGGGGGTGACCACCTTGCTGGTGTGGCTGCACAGTGTGT

+96

FIG. 22B

human	TTTGGGGGGCAGTGGGTGCAAGAGTT-TGGTTTGT-GTCTGCCGGCC- TT-GGGGAGCAGTGGGTGCAGCAGCC-TGGTCCTTGACTGCCAGC- TT-GGGGGGCAGTGGGTGCAGCAGCC-CGGTCCTTGACTGCCAGCCTG TTTGGGGGGGTGTAAAGCGGGAGGCTGGCTGTGCCCGCTGCTGACAGTCCGGCGTGT TTTGGGGG-GGAGGAGAAACAGAAAGTGG--GTAGAGCA-TGGACTCCCGCCCGCT	+150
human	AAACGCAACC-CACGCGGTGGGGGAGCGGC--TAGCGTG--GTGGA AGACACCGGC-CGTG-TGTGGGGAGCGGC--TAGCTCA--GTGGCCTTGGCCCGCGTG AGACACCGGC-CGTG-GGTGGGGAGCGGC--TAGCTCA--GTGGCCTTGGCCCGCGTG TACCTCGGGAACATGGTGTAGGGAAGCTGGAAGCAGATACGTGGAACCTCAACC-CAAG GATCCGTGTTACA-GCCGCAGATGGTGAGGCACTAG--AA-----	+205
human	GCCCTGTGGCAGCCGAGCCATGGTTTCT	+233
rat	GCCTGGCGGTAGAGGAGCCATGGTTTCT	
mouse	GC-TGGTGGCAGCGGAGCCATGGTTTCT	
chicken	AAACGCCAGCCTGAAGACCATGGTCTCG	
frog	----GGCAACAGACAGG--ATGGCGTCT	

FIG. 22C

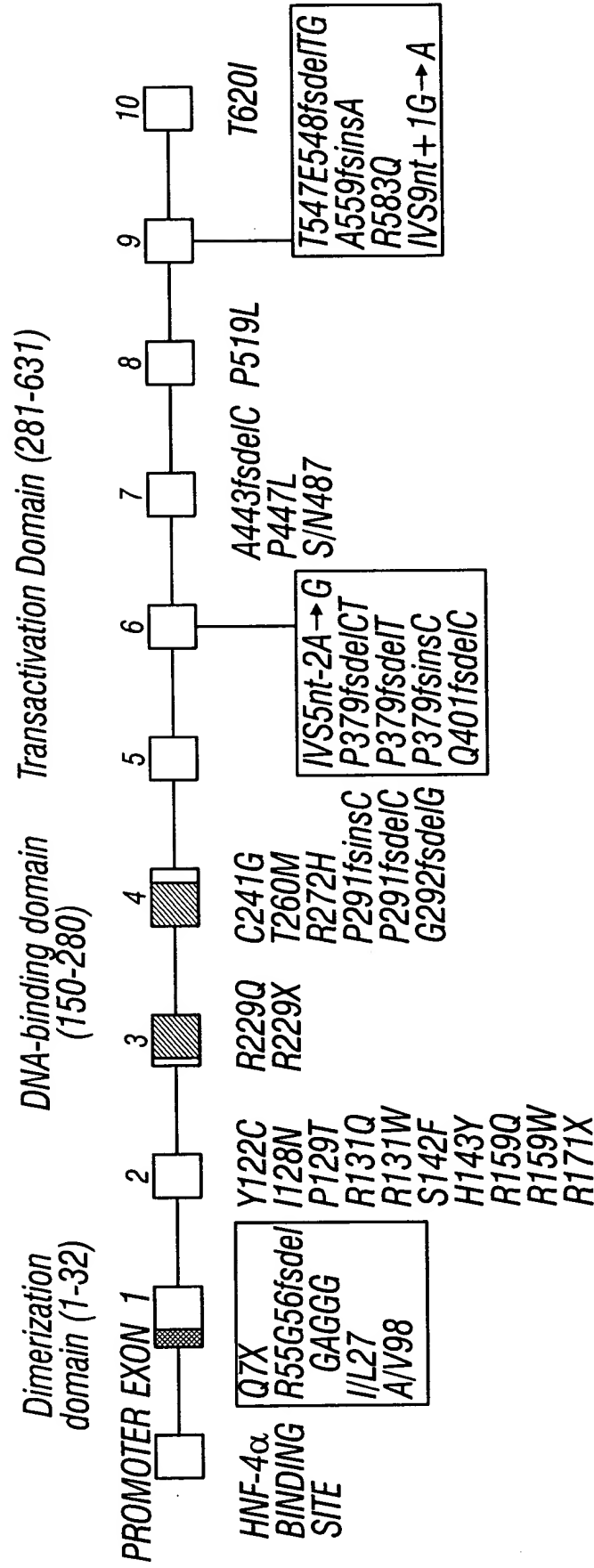


FIG. 23



J2-20

A	175	176	177	178	AT
	AAG	CAA	NGA	GAG	
	K	Q	R	E	
			X		

C/T

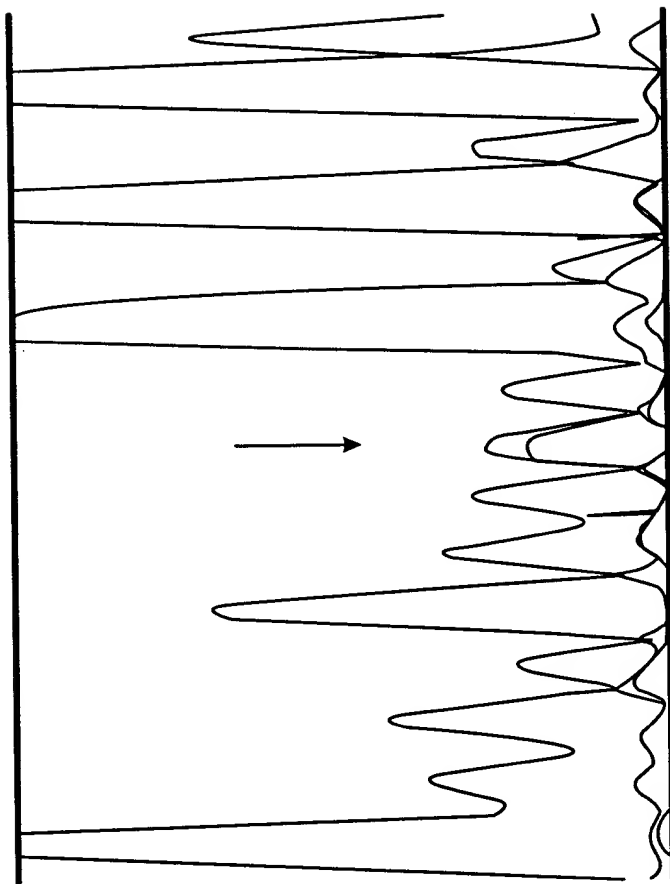


FIG. 24

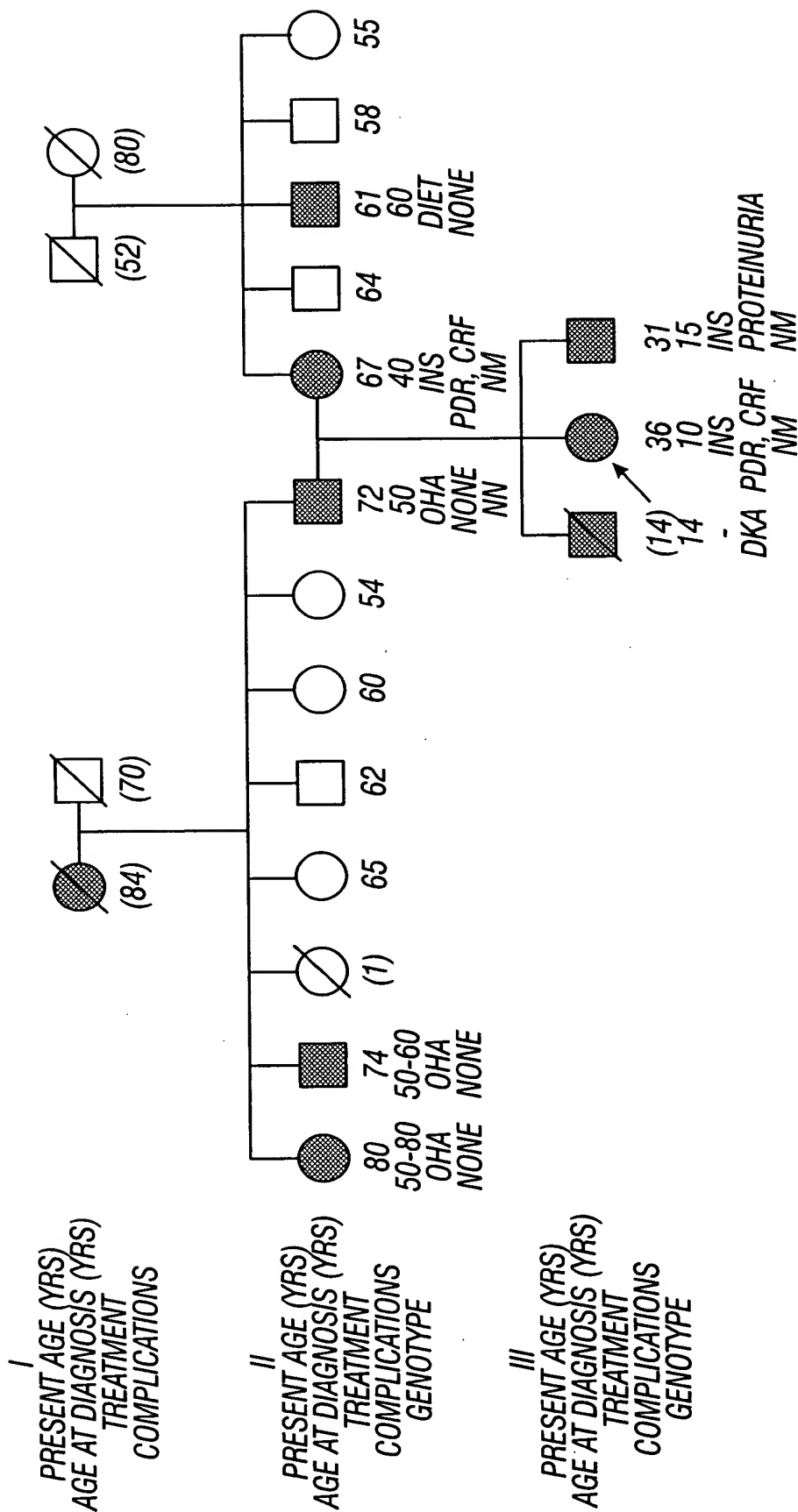


FIG. 25



	NF1	HNF - 3
1	<u>AGCCAGCACTGTTCTTGGCACATGGTAATCTTAACATAATTTTTCCTACAGG</u>	
91	<u>CCAAAATGGATGGAAGGGCCCAAAATGGCCGTGAGCATCCTCTGCCCTTGA</u>	NF1
		HNF - 3
181	CCGCTCTCGTAAGCAGCAAGCATTTTGTGGCTCTCCTGTCTCAGCATGATGCC	
	NF1	AP4
271	<u>CTCCTGATGGCTCCCTGGCTCCCAGCACCTTCCATCCCAGCTGCTCAGGGC</u>	
		AP4
361	TCCCATCGCAGGCCATAGCTCCCTGTCCCTCTCCGCTGCCATGAGGCCCTGCA	
	HNF - 3	C/EBP * Exon 1
451	<u>AAGCACCGGATAAATATGAACCTTGAGAAATTTCCCAGCTCCAATGTAAA</u>	
541	CCAGGGTTGGGGTTGGGGTGCCACAGGGCTTGGCTAGTGGGGTTTGGG	

FIG. 26A-1



AP1

GAGGCCTGGTGTCAAGGCCGGAGTGGGGTGGAAGGGTC

AP4

AP4

GAAGAGCTAGCCCAAGCTGTCTAGAGCTCCCTGCTGCTG

CCTACAAGGTTCTTTCGGGGGTGGGACCCAACGCTGCT

CCCTCACCTGCGCCTCCCCACCCCTCCCCCTCTGCCAC

HNF - 4 α

CTTTGCAGGGCTGAAGTCCAAAGTTTCAGTCCCTTCGCT

HNF - 3

AP1

CAGAACAGGCAGGGGCCCTGATTCAAGGCCGCTGGGG

GGGGCAGTGGGTGCAAGGAGTTTGGTTTGTGTCTGCCG

FIG. 26A-2



631 GCCGGCAGGCAACGCAACCCACGCGGTGGGGGAGCGGCTAGCGTGGTGACCCCGG

SerLysLeuSerGlnLeuGlnThrGluLeuLeuAlaLeuLeuGluSerGlyLeu
721 TCTAAACTGAGCCAGCTGCAGACGGAGCTCCTGGCGGCCCTGCTCGAGTCAGGGCTG

G

ProGlyProTyrLeuLeuAlaGlyGluGlyProLeuAspLysGlyGluSerCysGly
811 CCGGGGCCCTACCTCCTGGCTGGAGAAGGCCCCCTGGACAAGGGGAGTCCTGCGGC

GlyLeuGlyGluThrArgGlySerGluAspGluThrAspAspGlyGluAspPhe
901 GGGTGGGGGAGACTCGGGGCTCCGAGGACGAGACGACGACGATGGGGAAGACTTC

Val

SerProGluGluAlaAlaHisGlnLysAlaValValGluThrLeuLeuGln¹⁰⁹

991 AGCCCTGAGGAGCGGCCACACAGAAAGCCGTGGTGAGACCTTCTGCA gtaagg

T

FIG. 26B-1



¹MetVal
GCCGCGTGGCCCTGTGGCAGCCGAGCCATGGTT

Leu
SerLysGluAlaLeuIleGlnAlaLeuGlyGlu
AGCAAAGAGGCACTGATCCAGGCACTGGGTGAG
C

GlyGlyArgGlyGluLeuAlaGluLeuProAsn
GGCGGTCGAGGGAGCTGGCTGAGCTGCCCAAT

ThrProProIleLeuLysGluLeuGluAsnLeu
ACGCCACCCATCCTCAAAGAGCTGGAGAACCTC

agccctgccccgtccccgctcccaggagagccta

FIG. 26B-2



1081 gagggggccccctcagctcctaagagcccccccttctgagttgagttcc
1171 agggcccatgagagcccagggtccttgcttgagggtttgagcctcca
1261 ccaggccttagcccagtccttgggcnagggggacatttcccaggggg
1351 c::::::::: 9 kb ::::::::::: caccacccatccatccgtccat
1441 acatatctcatctgtgtgtgtgtgtgtatccatgtttctaaacc
1531 tttgtcatgtgtgcgtcnacaagtctctgtcctcatgaccatgtgt
1621 ccctgagtctatgttagggccctgggctccataactgctttcatgca
1711 ccgagccccacctatggggagagacagcccttgctgagcagatcccg
a

FIG. 26C-1



ccatgaccttcagcctttagccttagctgggaaggggac
gcccctgaactgctcctctgcagagtcaccaatcccatgagc
tccaagatgggagaaaaagcagtgaaattcacaactcaaatgc
ccaccattcatccattcatccattcaccatccatccatcc
tttatctgttccagtgtctgtatccataggcctgtgtccacg
ctgtgtccctgtgtcctggcataaatgaccatacctcaccgt
cagtccccaccctcag^gagttgacaagggtccagaccccagga

Exon 2 109 (G1) nGluAspProTrpArgValAlaLys
tccttgccctctcccag GGAGGACCCGTGGCGTGTGGCGAAG

FIG. 26C-2



MetValLysSerTyrLeuGlnGlnHisAsnIleProGlnArgGluValVal
1801 ATGGTCAAGTCCCTGACGACACAAACATCCCACAGCGGGAGGTGGTC
A (R131Q)

LeuAsnLysGlyThrProMetLysThrGlnLysArgAlaAlaLeuTyrThr
1891 CTCAACAAGGGCACTCCCATGAAGACGCAGAGCGGGCCGCCCTGTACACC
1981 taatgaccctaccccgcatcttccctgggagggcccaggactctcccctaa
2071 acagacaggtagatggaaaggaaagtcagtgggattcaacctgcatttatta
2161 ttgggtcctgaacatccaaagatgaatgaaatgggtccctgcttctcttttc
2251 ctggaaaaatatgtaagctctctgagcctcagcttcttcatctgtacaatg
2341 ttacctgcagtcttgtagtgagaaggatggtagagatcatatcttgggttgg

FIG. 26D-1



AspThrThrGlyLeuAsnGlnSerHisLeuSerGlnHis
GATACCACTGGCCTCAACCAGTCCACCTGTGTCCCAACAC

TrpTyrValArgLysGlnArgGluValAlaGlnG(ln)¹⁷⁶
TGGTACGTCCGCAAGCAGCAGAGAGGTGGCGCAGC gtaag

ctcataggctgggggctggaagcttcaccatccccattac

cctattctgcgccaggcactctgtgggacgggagtanac

tttttttagata::::: 3.8 Kb :::::cgtgact

gggataagtaaatgtgccaaatcagaacaaatgctaagc

taggaaagcattcagggattgattagtgatgtttgcctt

FIG. 26D-2

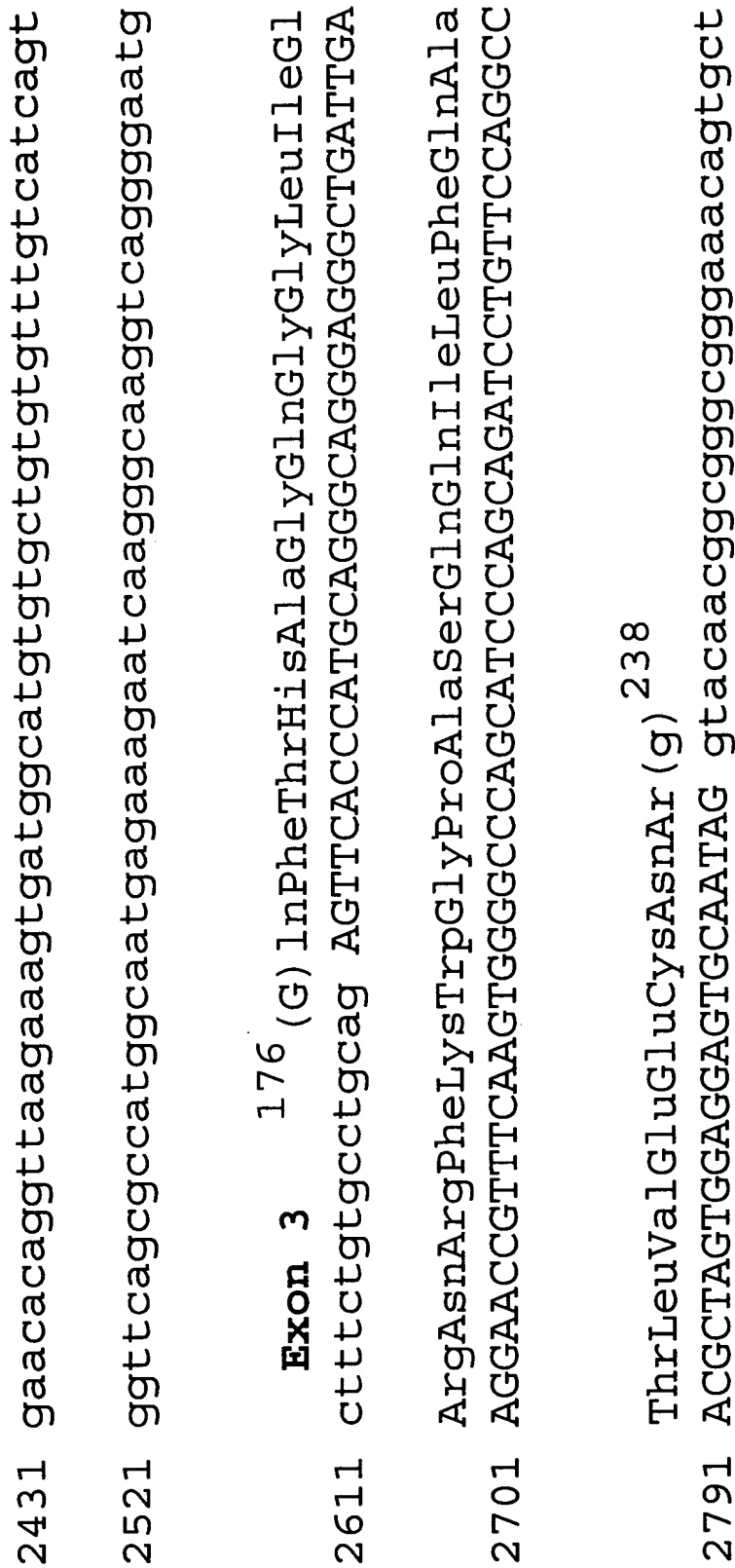


FIG. 26E-1



agattagatgatttctaagttctagctgtaagctcctct

gacgaggaaggtgagagtggccagtagccactcacggt
t

GluProThrGlyAspGluLeuProThrLysLysGlyArg
AGAGCCACAGGTGATGAGCTACCAACCAAGAGGGCGG

TyrGluArgGlnLysAsnProSerLysGluGluArgGlu
TATGAGAGGCAGAGAACCCCTAGCAAGGAGCGAGAG

TA (R229X,
R229Q)

ggtttggtctgggctgcggcaaggccagggaagggaag

FIG. 26E-2



2881 gtgactctaggctcctgtaaaaggctgtccagttgccgagaactcctgatat
c

2971 taagccattcctcgagccccctgcacctggacaccaagcaaccctt

3061 atggctctttgctcactttatgaatggagagactgaggtcagacagactg

3151 cccagatctgccagcctcaaacctccggcagagntcagcttctcagaacc

Exon 4 ²³⁸ (Ar) gAlaGluCysIleGlnAr
3241 cctggaggctcatgggtggctatttctgcag GCGGAA**T**GCATCCAGAG
G (C241G)

euValThrGluValArgValTyrAsnTrpPheAlaAsnArgArgLysGlu
3331 TCGTCACGAGGTGCGTGCTACAACTGGTTTGCCAACCGCGCAAAGAA
A (R272H)

FIG. 26F-1



tggcttagcctggcccagaaaaattgagaatacttgaacc

ccatggatgctcacccaattcgattctctctacaatcct

tcaattgcccagggtcacacagcagacctggcattggaa

ctcccccttcatgcccaggacaggggttcctctgagcctgg

GlyValSerProSerGlnAlaGlnGlyLeuGlySerAsnL
AGGGGTGTCCCCATCACAGGCACAGGGGCTGGGCTCCAACC

GluAlaPheArgHisLysLeuAlaMetAspThrTyrSerG
GAAGCCTTCCGGCACAAAGCTGGCCATGGACACGTACAGCG

FIG. 26F-2



lyProProGlyProGlyProGlyProAlaLeuProAlaHisSerSer
3421 GGCCCCCCCCAGGCCAGGCCGGACCTGCGCTGCCCGCTCACAGCTCC
C [^](P291fsinsC)
isG(ly) ³¹⁹
3511 ACG gtaagtggatatgtgggacaaggacacgtgggaaggtgggaaggt
3601 ttgcacgtcagtttggttccattc::::: 2 kb ::::::gcagct
3691 gctggctgcataaaggcagacaggcagatggcctaagcaaaccaatggag
Exon 5 ³¹⁹ (G) lyValArgTy
3781 aagtgggtgctgaggcaggacactgcttccctctccag GTGTGCGCTA
erSerGlyGlyProLeuValThrValSerThrProLeuHisGlnValSer
3871 GCAGCGCGGTCCCTTAGTGACAGTGTCTACACCCCTCCACCAAGTGTCC

FIG. 26G-1



ProGlyLeuProProAlaLeuSerProSerLysValH
CCTGGCCTGCCCTCCACCTGCCCTCTCCCCCAGTAAGGTCC

tggggaggactgtcccattgacagcagtcacctaaccctct

gaccagggtattggcaaaaggtagaaacaaaggcagattt

tttgaagtgtgagggtgtggaggcaggggagggcaggg

GlyGlnProAlaThrSerGluThrAlaGluValProSerS
TGGACAGCCTGCGACCACTGAGACTGCAGAAAGTACCCTCAA

ProThrGlyLeuGluProSerHisSerLeuLeuSerThrG
CCCACGGCCTGGAGCCCAAGCCACAGCCTGCTGAGTACAG

FIG. 26G-2



luAlaLysLeu³⁶⁹
3961 AAGCCAAGCTG gtgagtgtccttgcttgtaaggaaa

4051 cctgtgggacccccggccccgacacagcttggct

ThrAlaLeuHisSerLeuGluGlnThrSerProGly
4141 ACAGCACTGCACAGCTTGGAGCAGACATCCCCAGGC

FIG. 26H-1



acccaacctcatcttcccttggcaggagattcttgagcagtccttagggaggc

Exon 6 ³⁷⁰ValSerAlaAlaGlyGlyProLeuProProValSerThrLeu
tccccctcgtag GTCTCAGCAGCTGGGGCCCCCTCCCCCTGTCTCAGCACCCCTG
g (IVSnt-2A-G) (P379fsdel1CT)

LeuAsnGlnGlnProGlnAsnLeuIleMetAlaSerLeuProGlyValMetThr
CTCAACCAGCAGCCCCAGAACCTCATCATGGCCTCACTTCCTGGGGTCA TGACC
(Q401fsdel1C)

FIG. 26H-2



IleGlyProGlyGluProAlaSerLeuGlyProThrPheThrAsnThrGly
4231 ATCGGGCCTGGTGAGCCTGCCCTCCCTGGGTCTACGTTCAACCAACACAGGT
4321 gggcacctgggtgggaggctcatggggcaaccgcanaatccaggagctgga
4411 caacatgt::::: 0.8 kb :::::taggagaggggagcagagaactg
4501 caggaaccgcagtttgacaaactttgaacaagtcaaccgcttgcttttccc

FIG. 26I-1



AlaSerThrLeuValIleG(ly)⁴³⁷
GCCTCCACCCCTGGTCATCG gtaagctggtggggatgggt
aaagccactgggactcattcattcattcattcattcata
accccatggcctttgcactgctgtgtaccccgaggctc
attagcttagacaaagagctaaaggctcagagagggga

FIG. 26I-2



4591 atgacttgccagagccacttaaattagtggcaggtcccagtgaggaggctg

4681 tgggaaggagaggtggtgcccttgggaggtcttgggcaggggtgggatat

Exon 7

437 (G) lyLeuAlaSerThrGlnAlaGlnSerValProValIleAsnSerMetGly
4771 GCCTGGCCTCCACGCAGGCACAGAGTGTGCCGGTCATCAACAGCATGGGC

T (P447L)

roLeuHisProSerTyrGlnGlnProLeuMetProProValGlnSerHis
4861 CGCTGCACCCCTCCTACCAGCAGCCGCTCATGCCACCCTGTGTCAGAGCCAT

FIG. 26J-1



tttcctgaccaccttgcccccttcttccaaccacgggctc

aactggggggccagctgattccctcccccttccactccag

SerSerLeuThrThrLeuGlnProValGlnPheSerGlnP
AGCAGCCTGACCAACCCCTGCAGCCCGTCCAGTTCTCCCCAGC

T

Ser

ValThrGlnAsnProPheMetAlaThrMetAlaGlnLeuG
GTGACCCAGAAACCCCTTCATGGCCACCATGGCTCAGCTGC

G

FIG. 26J-2



gaggttggctgtcaatggatgcaggggaaaggggtgcct
gagggtgtctgcaggccagtggtgttcccatgtgaatgc
tctgggtgtgtatcgggttgatgcatttgtgtgcat
aga::::: 1.5 kb :::::ccagttttgaaaatc
ccccctttcccagtccttgaggcctgggactagggctg

FIG. 26K-2



Exon 8

5401 tcaggcacggttgccacgtctgccccctctctccccctg
yLeuLeuProGlnThrMetLeuIleThrAspThrThr
5491 CCTGCTCCCGCAGACTATGCTCATCACCGACACCACC
5581 tgctggccctccctcggcctgtgacagagccccctcac
rAspThrGluAlaSerSerGluSerGlyLeuHisThr
5671 AGACACTGAGGCCCTCCAGTGAGTCCGGGCTTCACACG
(T547E548fsdelTG)

FIG. 26L-1



501 (A) laLeuTyrSerHisLysProGluValAlaGlnTyrThrHisThrGln
cggccag CCCTCTACAGCCACAAGCCCGAGGTGGCCAGTACACCCACACGGG

A

AsnLeuSerAlaLeuAlaSerLeuThrProThrLysGln⁵⁴¹
AACCTGAGCGCCCTGGCCAGCCTCACGCCACCAAGCAG gtaagggtccaggcc

Exon 9 542ValPheThrSe
ccccacatccccggggtcaggaggctgctctgctccccccag GTC TTCACCTC

ProAlaSerGlnAlaThrThrLeuHisValProSerGlnAspProAlaGlyIle
CCGGCATCTCAGGCCACCACTCCACGTCCCCAGCCAGGACCCCTGCCCGGCAT

FIG. 26L-2



eGlnHisLeuGlnProAlaHisArgLeuSerAlaSerProThrV
5761 CCAGCACCTGCAGCCGGCCACCGGCTCAGCGCCAGCCCCACAG

5851 tccatgttggtcccaccccttctgttgctgccgtcactgtgggg

5941 ggcgtggaagggtggggtggcttccatgaa::::: 1.5 kb

6031 gcggccgtggaccctggctggaggctcccttctgttaagaaccg

6121 ggaggtgtggccctgcctcccatcctgagtagccctagggaca

Exon 10 590 (V) alserSerSerLeuValLeuTyrGl
6211 gtttgcctctgcag TGTCTCCAGCAGCCTGGTGCTGTACCA

sSerValIleGluThrPheIleSerThrGlnMetAlaSerSer
6301 CAGCGTCATCGAGACCTTCATCTCCACCCAGATGGCCTCTTCC

6391 GGGGGGT

FIG. 26M-1



(a1) 590
gtgagagccctgggtccacccccctcccttactgtccctgccccct
a(IVS9nt1G-A) t
ctgtgcatgcagcaggcctagggtgctgtgaggaagcactggca
:::::tccagtgtcacagtaagatgtactcaggccagtcctatgg
agggtagagggtgtgactttggggttcctgttatgtgctgtgatcca
ggcagggtggggtgtgggtgcctgggtgggtggctagcagcctt c
SerSerAspSerSerAsnGlyGlnSerHisLeuLeuProSerAsnHi
GAGCTCAGACTCCAGCAATGGCCAGAGCCACCTGCTGCCATCCAACCA
SerGlnOC⁶³¹
TCCCAGTAACCACGGGCACCTGGGCCCTGGGGCCTGTACTGCCTGCTT

FIG. 26M-2



PrF

CATGAACCCGAAGAGTAGTGTCTTCTCTCTGGACTAAGCGGAACCTGAGAACCGGTGGA

GGCTGATAAGCAGAACCAAGTAAAGAGGTCTCTAGCCCCCAGCGTGAGTACAATGGAC

CCCTCTCTCCGGGTTTCCCCCTCCCCACCATCATTTTGCAATCCAGCCGAAAGCTGGGCCCT

PrR

TTTTCTGACTCCTTTCGGAGGAGCCTCCGGGACCCCGGGAGTAACAGGTGTCTGGAGGC

1

Met Val

TCTCGCACCCACCCCTCACCCCTTCTTTTCCGTCCTTGAAA ATG GTG

Ser Ser Gly Val Thr Lys Glu Val Leu Val Gln Ala Leu Glu Glu
AGC TCC GGG GTC ACC AAG GAG GAG GTG CTG GTT CAG GCC TTT GAG GAG

Ex1-1R

Leu Ser Pro Gly Ser Gly Ala Glu Pro Asp Thr Lys Pro Val Phe
CTG TCC CCT GGC AGC CGG GCC GAG CCC GAC ACC AAG CCG GTC TTC

FIG. 27A-1



AAAGCCCGCCTAGGCTGCAAGGCACTGGCTTAACAAGTCCAAGTTAGGTGAAGTTT

CCTGGCAAAGCCCGCTCCCGGCCAGGTCTTCTGCTCTCCAGGTCTGCCCTCCGGCTCT

Exon 1 - 1F

TCCCACTAATTGCAATCTTATATGCGCCTAATGGTGGCGATCATGGCAAGTT AGAAG

Exon 1 - 2F

TGAAGGTGGAGGGTTCTGGATTGCGGTTTGCTTGTGAAACTCCCCCTCCACCTCCTC

Ser Lys Leu Thr Ser Leu Gln Gln Glu Leu Leu Ser Ala Leu Leu
TCC AAG CTC ACG TCG CTC CAG CAA GAA CTC CTG AGC GCC CTG CTG CTG

Leu Leu Pro Ser Pro Asn Phe Gly Val Lys Leu Glu Thr Leu Pro
TTG CTG CCA TCC CCG AAC TTC GGG GTG AAG CTG GAG ACG CTG CCC

His Thr Leu Thr Asn Gly His Ala Lys Gly Arg Leu Ser Gly Asp
CAT ACT CTC ACC AAC GGC CAC GCC AAG GGC CGC TTG TCC GGC GAC

FIG. 27A-2



Glu Gly Ser Glu Asp Gly Asp Asp Tyr Asp Thr Pro Pro Ile Leu
GAG GGC TCC GAG GAC GGC GAC GAC TAT GAC ACA CCT CCC ATC CTC
115
Ala Glu Val Asp Arg Met Leu Se(r)
GCG GAG GTG GAC CGG ATG CTC AG GTAGGCGCAGAGCCAGGTGGAGGGACCC
Ex1-2R
AAGCCCGTTTCCACCAAAATAATCCCCGGGGGCGCTCTGCTTCTCTCCCAACACCCG
CCAGGCCATCGTCC::: 9 kb :::::TCAGAAAGAAAGGATGAGGTGTACCG
GTTGTAGCTTAGATGGGGGAAATTCAGAAATTTGCATAGACCATAGGTAGCACCCCT
115
2 (Se)r Glu Asp Pro Trp Arg Ala Ala Lys Met Ile Lys Gly Tyr
CTAG T GAG GAC CCT TGG AGG GCT GCT AAA ATG ATC AAG GGT TAC
Gly Leu Asn Gln Ser His Leu Ser Gln His Leu Asn Lys Gly Thr
GGC CTG AAC CAG TCG CAC CTC TCC CAG CAT CTC AAC AAG GGC ACC
182
Arg Lys Gln Arg Glu Ile Leu Arg G(ln)
AGA AAG CAA CGA GAG ATC CTC CGA C GTAAGTGTTTTCATCCTGCCTCTGCC

FIG. 27B-1



Lys Glu Leu Gln Ala Leu Asn Thr Glu Glu Ala Glu Gln Arg
AAG GAG CTG CAG GCG CTC AAC ACC GAG GAG GCG GAG CAG CGG

ACCCGAACCCCTGGAGCCCCCGGGCCCTGAGTGACACTGCGCCCGACACACTCGCC

GACCCCTTCCCAATCCCTTAGCGGGACAACCCCTGCGGCCACCGGCTTCTTCTCCCCAGGC

TACAGGGCAGTCACCTTCTCCTCTGTTTAGCTTCCATTTTGGCCTCATGTCTACCCCAA

Ex2F

Exon

AGAAAAAGAAATGTTTCTCCCCAGATGTCTCCCACTAGTACCCTAACCATCTGCTTGTCTGT

Met Gln Gln His Asn Ile Pro Gln Arg Glu Val Val Asp Val Thr
ATG CAG CAA CAC AAC ATC CCC CAG AGG GAG GTG GTC GAT GTC ACC

Pro Met Lys Thr Gln Lys Arg Ala Ala Leu Tyr Thr Trp Tyr Val
CCT ATG AAG ACC CAG AAG CGT GCC GCT CTG TAC ACC TGG TAC GTC

Ex2R

TCAACCTGAAGTGACCTTTTGCCCTCTCACCCCATTTGGCTGCCCTCAGTTTCCCTTTCATCGAC

FIG. 27B-2



AAGGCCCTTGAGCACTTGGCAGATATGAGGAAGGTGGCAAGTAGATTGGCCCTTGGTG

CAGTTGCTCTGAGGAGCCTGTCAGTGT::: 5 kb ::::: GATTGAGCTCAC

GAGCCAAGGGGAAAAATAATTTCTTAAACTATAGCTGGCTATGTTTGAGCTC

CTGAGGGCTCCCATCTCCAGCTCCACATGCAGTGAGAGAAGGTTGCCAAGCTTAGTTA

182

EX3F

Exon 3 (G) In Phe Asn Gln

GAAGGCTACAGACCCTATCAAATCTACTCCTTTCTCTTTTCAG AA TTC AAC CAG

(G) In

Gln Leu Leu Phe Phe Pro Glu Phe Ser Gln Gln Ser His Gly
CAG CTG CTG TTT CTC TTT CCA GAG TTC AGT CAA CAG AGC CAT GGG

FIG. 27C-1



GTTGCTGTACAATGGATTGGCTTCTGTCAATGTTCTTTCAGTCAAGCCCCCTTGCTACCCAGC

CCACTTGACATCAAATACAGGAGTTCAGGATGCAGAGTGTGCTTCATCTCTGAAGGCCAGT

CTTCAAAGAAAGGAAAGGGTGGCTTTGCTGGAGCAACTGAGGTGGCAGTAAGGGCCTGTG

GACGAGGGGAATAAACCTGTCTTTCGTCGTTGTCTGTCTGTCTGTCTGTCTGTCTGTGAGT

Thr	Val	Gln	Ser	Ser	Gly	Asn	Met	Thr	Asp	Lys	Ser	Ser	Gln	Asp
ACA	GTC	CAG	AGT	TCT	GGA	AAT	ATG	ACA	GAC	AAA	AGC	AGT	CAG	GAT

Pro	Gly	Gln	Ser	Asp	Asp	Ala	Cys	Ser	Glu	Pro	Thr	Asn	Lys	Lys
CCT	GGG	CAG	TCC	GAT	GAT	GCC	TGC	TCT	GAG	CCC	ACC	AAC	AAG	AAG

FIG. 27C-2



Met Arg Arg Asn Arg Phe Lys Trp Gly Pro Ala Ser Gln Gln Ile
ATG CGC CGC AAC CGG TTC AAA TGG GGG CCC GCG TCC CAG CAA ATC
270
Arg Glu Ala Leu Val Glu Glu Cys Asn Ar(g)
AGA GAG GCC TTA GTG GAG GAA TGC AAC AG GTAACACCACCAAGCTCAGG

CACTAGTTATACAGATAAGTGTGGCTAAATCAGAGCTTCTCAAAGTATGTTCCACA:::270

Exon 4 (Ar)g Ala Glu Cys Leu Gln Arg
CCTTCACTCACCATCTCCCCTCCATCCATCCAG G GCA GAA TGT TTG CAG CGA

Thr Glu Val Arg Val Tyr Asn Trp Phe Ala Asn Arg Arg Lys Glu
ACT GAG GTC CGT GTC TAC AAC TGG TTT GCA AAC CGC AGG AAG GAG

Gln Thr His Ser Leu Asn Pro Leu Leu Ser His Gly Ser Pro His
CAG ACT CAC AGC CTG AAC CCT CTG CTC TCC CAC GGC TCC CCC CAC

FIG. 27D-1



Leu Tyr Gln Ala Tyr Asp Arg Gln Lys Asn Pro Ser Lys Glu Glu
TTG TAC CAG GCC TAC GAT CGG CAA AAG AAC CCC AGC AAG GAA GAG

EX3R

TGGGCAGGTGGCAAGTACACAGACCCAGGAACCTCCCCCTCGGTCTGGGATATTGAGA

EX4 - 1F

2 kb ::::::::::GTGATTGTGTGTTTGGGCCAAGCACCAAGTCCCCCGCCCC

Gly Val Ser Pro Ser Lys Ala His Gly Leu Gly Ser Asn Leu Val
GGG GTG TCC CCC TCC AAA GCC CAC GGC CTG GGC TCC AAC TTG GTC

EX4 - 2F

Glu Ala Phe Arg Gln Lys Leu Ala Met Asp Ala Tyr Ser Ser Asn
GAG GCA TTC CGG CAA AAG CTG GCC ATG GAC GCC TAT AGC TCC AAC

349

His Gln Pro Ser Ser Ser Pro Pro Asn Lys Leu Ser G(ly)
CAC CAG CCC AGC TCC TCT CCT CCA AAC AAG CTG TCA G GTAAGCAAAGGT

G K Q R

FIG. 27D-2



EX4-1R

TGGGCTCAGTGCCTCGGCAACCAACCATCCTGGTTCTTGCCACGGATCTTATCTGGT
L G L T A S A T Q P S W F L P R I L S G

GAATATACTCCCCTGGAAATAATGTGTGGCTCTGATCAGTT::: 3 kb ::::

N I L P W K O C

399

GCGCTTACATTCTAGAATTAAATAGAGAAACATGCCATATTACCTGGAGAAAGCAGC

EX5F

TGAAACAAGAGGTGCCGAGTCAATTGTTCCAGGACCCCTGGTGGCACTAATGTTCCCTAC

Glu Ile Thr Ser Ser Ser Thr Ile Ser His His Gly Asn Ser Ala
GAG ATC ACT TCC TCC TCA ACA ATC AGT CAC CAT GGC AAC AGC GCC

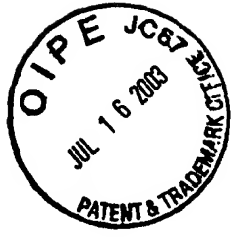
402

Leu Asp Pro Gly His Asn Leu Leu Ser Pro Asp Gly Lys Met
CTG GAC CCA GGC CAC AAT CTC CTC TCA CCT GAT GGT AAA ATG GTG

CTCACAAGGCCTGCCTCAACAATGAACCATTTGTAGCCCCCATAGGGGAAATGAGGGCT

::: 5 kb ::::: CCCAAAGTGATGGATTACAGGGGTGAAGCACCATGCCAGCCA

FIG. 27E-1



TTAAGGGTTTTCAGAGGAGCAAAACGCTTTTGAGATGATCCTAGGGCCGCTCTCTCATTTGCCA

L R V F R G A N A F E M I L G P L S H C Q

CCAAGGCACTGGGGATACATCAGTGAACAAACAAACGAGATAAAATTTCCTGCCCTCGTG

CGATATTCTTGTGGTGACAGGGGAGGAGAAAGCAACTTTATTCTTATTACCCACCCT

349

Exon 5 (G)ly Val Arg Tyr Ser Gln Gln Gly Asn Asn
TGGGTTTGTGTTGTTTGCAG GA GTG CGC TAC AGC CAG CAG GGA AAC AAT

Met Val Thr Ser Gln Ser Val Leu Gln Gln Val Ser Pro Ala Ser
ATG GTG ACC AGC CAG TCG GTT TTA CAG CAA GTC TCC CCA GCC AGC

EX5R

AGTACACCTGGGCCATTGTCGCTCTGGAGCTGATAAGATAAGAGGCAAAACAAACAACCTT

GTCCAGAGTCGGAAAGGAGAGGTAGTGCTGCTGAGCCCAACCTTTGGCGGGTAGAAAA:::

ATAATTGTTATTGAGTGAATGAAGGAATGAATTGAGAACTAGTCATGCCAAGGAATCGCTA

FIG. 27E-2



EX6F

AGTCACATCGTGTGGAAACTGCTCTTTGTGGTCCAAGTCCACCCATGTTTCTCTTGT

Ser Thr Leu Thr Asn Ile His Ser Leu Ser His His Asn Pro Gln
AGC ACC TTG ACG AAT ATC CAC AGC CTC TCC CAC CAT AAT CCC CAG

447

Ile Ala Gln S(er)

ATT GCA CAA A GTAAGTTCTATTCTTGGTTGGAAACCTGGGGCAGGAGAGAA

TAGTAAATTGGTTAACTTCTTTAGTTTCTCATCTGTCTCCTTAAATCCAATATTGG

AGCTGTGCATCCTGGGTCAAATCATTGAACCT:::::4 kb :::::::ATGACTC

FIG. 27F-1



403

Exon 6 Ile Ser Val Ser Gly Gly Gly Leu Pro Pro Val
TTTTTCTCTCCATCAG ATC TCA GTC TCA GGA GGA GGT TTG CCC CCA GTC

Gln Ser Gln Asn Leu Ile Met Thr Pro Leu Ser Gly Val Met Ala
CAA TCT CAA AAC CTC ATC ATG ACA CCC CTC TCT GGA GTC ATG GCA

EX6R

GAATGGGAAGCAAATTAAATGTGGTGAAATAAATACTGTAGGTCTCCTTCAAACTCACCACAAC
ATTGTTAGCCTAAACAAGAAAAAATTGTGGAATGGATTGGAATCCTGTGCACAGTTTAGC
TGGGAGACTCTCAGGCTTTAATCAGATCTGTTTAATGCCCATCTCCAACCCACAACACTCATTG

FIG. 27F-2



TGGAACCTTGAGCAAGTAAATTAATATCTCCAAGTCTCCGTTTCTTTACACTTGCCCTCCCATGG

EX7F

Exon 7

ATGGCATCCATCCACCTCTCCTTATCCAGGAGCTGTCTGTCTTTTCCCTCTTGCTCCCCACA

Ser Val Ala Gly Ser Leu Ala Ala Leu Gln Pro Val Gln Phe Ser Gln
AGT GTG GCC GGC AGC CTG GCA GCC CTG CAG CCC GTC CAG TTC TCC CAG

Pro Gly Ser His Met Ala Gln Gln Pro Phe Met Ala Ala Val Thr Gln
CCA GGC AGC CAC ATG GCC CAG CAG CCC TTC ATG GCA GCT GTG ACT CAG

EX7R

GGACCCCTCAGTGGCCAACCACTTTCCCTCTCTGGGTCTGAACCTTCTCGGAAGTTTATTGGCT

TGAGTGTGCTGTACCTTTTCTAGTCCTTCTCTACCCCTGAGATTCCCAGGAAGGTTTG

GGTAGGAAATGTGTCTGAGAGCAGGTGTTTCTCCCTCACAGCCAAGCATCCACATGCTTTC

ATCCCCACTATAACCAACAGCCCTTTTATCTACCTGAGGAGATGGAGCTATGGTGTGGGATG

FIG. 27G-1



AATCTCCTATGTAAACAGGCTCAGCCCGTGACTGGACATTGAGCGGGGCTCAAATG

447

(S)er Leu Asn Thr Ser Gln Ala Gln Ser Val Pro Val Ile Asn
G GC CTC AAC ACC TCC CAA GCA CAG AGT GTC CCT GTC ATC AAC

Gln Leu His Ser Pro His Gln Gln Pro Leu Met Gln Gln Ser
CAG CTG CAC AGC CCT CAC CAG CAG CCC CTC ATG CAG CAG AGC

512

Leu Gln Asn Ser His M(et)

CTG CAG AAC TCA CAC A GTAAGACACGGGCATGTGGAGGGAGGAGCACTCA

TGGTCACTTTCCCTATGATCAACCGACTAAGACAATTCTCAAGCATAACTCT

AA::::::::: 2 kb ::::::::::: TGACCTTTGCTCCCGTTCCGTACCGAGGCCTCCCT

GGGAGTTGGTTATGTGACTTGGAATTTACATGAATCTTATGGATAACTAATATGAGAA

EX8F

GGGGCTCTGTACCTGTGTCTTTGGCCTGTGTATGCACCTTGATTCTGTCTTCACTCTGT

FIG. 27G-2



512

Exon 8 (M) et Tyr Ala His Lys Gln Glu Pro Pro Gln Tyr Ser His
CTCTCCAG TG TAC GCA CAC AAG CAG GAA CCC CCC CAG TAT TCC CAC

551

Ile Ser Thr Leu Thr Asn Met Ser Ser Ser Lys Gln
ATC AGT ACA CTC ACC AAC ATG TCT TCA AGT AAA CAG GTAATGCCAGCAG

EX9F

GGCAAGCATGGACTCGGCCAGAAATTATATCCT::::: 10 kb ::::::CTTTGCTG

552

Exon 9 Cys Pro Leu Gln Ala
TGACACAGCTGAGCACCCCTCTCTCCTCTCTCTCTG CAG TGT CCT CTA CAA GCC

EX9R

CCATCACCCCTCTGGGCAGCTGTTCATGGAAAAGCCAGTGACCTGACCAGCACCTGCGAGAG

FIG. 27H-1



Thr Ser Arg Phe Pro Ser Ala Met Val Val Thr Asp Thr Ser Ser
ACC TCC CGG TTT CCA TCT GCA ATG GTG GTC ACA GAT ACC AGC AGC

EX8R
GATATCGGGGGTTGGGGTGTGGGCAGGGTGTGATAAGGCCATGGATGTGCAAAGGTTGT

GTTGAGTTGGGCATCATCTCCCTTAGAGAAAGCCAAACTAATGGCCCATGACCCCTGCCAAA
557
Trp OP
TGG TGA TGCCACACACCACTTACTTCGTGCGCAACAACAAGGACCCTGTTTCCACA

GTCCCTGCTACCTGACGGACGTCCTGCTGGCACCTCAGACAAATCCACTCTCAGGAGGCGCA

FIG. 27H-2



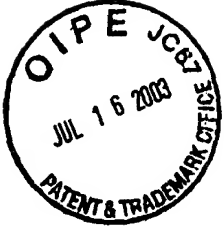
GCCCGAAGCCAGTTTCCCTTCTATGCAGTATTGCCACAATGCCCTCTCCCACGATGTCAA
GTACTGTCTATGTTGTGATCCTTCA TCGAACA AACTGATGCGAAAACTTGAATCTGTAC
AGACTCCCTCCCTGCCCCCATCCCACATGATCTTGAGATTTC TTTTAAAGATAAATT
TCCCTCTGCCCTGTATATAATACTAAAGTGTCTATTAGTTTCTTTGTAAAGTCAAG
TGAAGCCCTTGTCTCTCCCGGGCCCTGGACACTTATGGGGACAGCATACCTTGGACT
TGAATGTAGTGTGCAGAGTAACATGCCAGCTTCCTGTGGGCCAGGAGCTCAGCCTGCAC
CTCAAAAGCCTTCCATTAAACAATTATTATTTATCACTAAAAAAA

FIG. 27I-1



GGACTCCTGTCTGTCCCTGGAGGTGGAGACAAGGAACCAACCGAAGAGGAAAGCAAGAAAGCC
TGAAATGAGGAGAGAGACATGTGCTATTGAACTGAGCCAAACACACTGTAAATATCCAC
TGTCCAATGGCTGTAAACTATAAATACTGTAAATTAAGTGCAATTTCCTCTGTGTCTCCTC
TCAAAAATTCAAAAGTGATCTGTCCCCCTCTCCCTCATGGAGAAACATCCTAAGTGGGAAG
GACTACCAGCTAACTCCAGTCTCCTGACATTAGACACACCTCTGGATCCCTGGAGGGGC
TCCCTAAGAAACCCAGGGCAGGGAAACTGGCTGTTTGATAGCAGAGAAAGTTGCAGT

FIG. 271-2



1 TGGGTTGCCCTGTGACTGCACTGGCGATACCCCAAGCCCACTCT
91 GGATACGAAACAGGGAGAGGAGGGGGAAGAGGATGGACGTCTA
181 CTCAAACCAACCCTTTGAAGTTGATTGTACATTTTACAGAAAGGAAA
271 GTAGACGGTAGGTGCCCTGAATGTAAATCCAGGTCTCTGCCCTGCTCCG
361 ATCCGAGATGGAGCCAGCCTGGGCCAGAAACACTGGGAGCTGTGGGA
451 AATTGGAGGTGAATCTGGCCCTCCCAAACTTCCAGTCCATTCTGCTC

FIG. 28A-1



GAAGGTAGGAGACGGGTGGAGAGAAACAGGGGATGGCAAGGG
CCAGGCCCACTTGGTGCTTGATTTATGCCATCTCATTTCCCTT
CTGAGGCTCGGAGAGGAGAAATCATTTACCCAAGTCCCAGTTA
GGGAGGGGTGGGGTGAGGGAAACAGGAGAAATGTGATGGGAAA
GACGAGAGGGGCAGGGTGGGATCACAGGAGCAGGAGCGGGG
CCAGGGAAACCGGAAACTGCGGGGAACTGGAAGGAGCTCC

FIG. 28A-2



P1F →
541 CAGAAACAAGGATCCAGAAAGATTGGCATCTGGGGCCCTGGGATTTAGGTTTC
HNF - 6
631 ATTGAGGGTAGAAGTCAATGATTGGGAAGTTATTGAATTAGGGGATCTC
721 CCTGACTTGGGGTGACAAATGGCTTGGAGGGGTGGGTGAGTCAAGGGTCAA
811 ATAACTGAACATCGGTGAGTTAGGGCCCCAGCAGTTGTAATTAGCACCCC
HNF - 10
901 GCCCGCCAGCCTATCCACCGCGGGGACCGATTAAACCATTAACCCCC
A
991 GGCCAAGACTCCAGCAGATCTTCCAGAGGACGGTTTGAAAGGAAGGCA
*
← P1R

FIG. 28B-1



TAAATCGTGGGCCATGGGGCAGCCTTATCTCTGCAAAAGC

GGAGGTAGGCTGTCAGTGCCCTGATAGTATCAGTTAGAATG

P2F →

ATGAGTGCCCGTGAGTCATGATGCCCTTGCTGTACAATTG

HNF - 3

GGGTGTCAGCCAGAAACCAACACAGCCAAATCCCTGCA

ACCCCTCCCGCAGAGCCTCCACCCCTTCACAGAGGCTA

E1F →

GAGAGGGCACTGGGAGGAGGCAGTGGGAGGGCGGAGGGCG

FIG. 28B-2

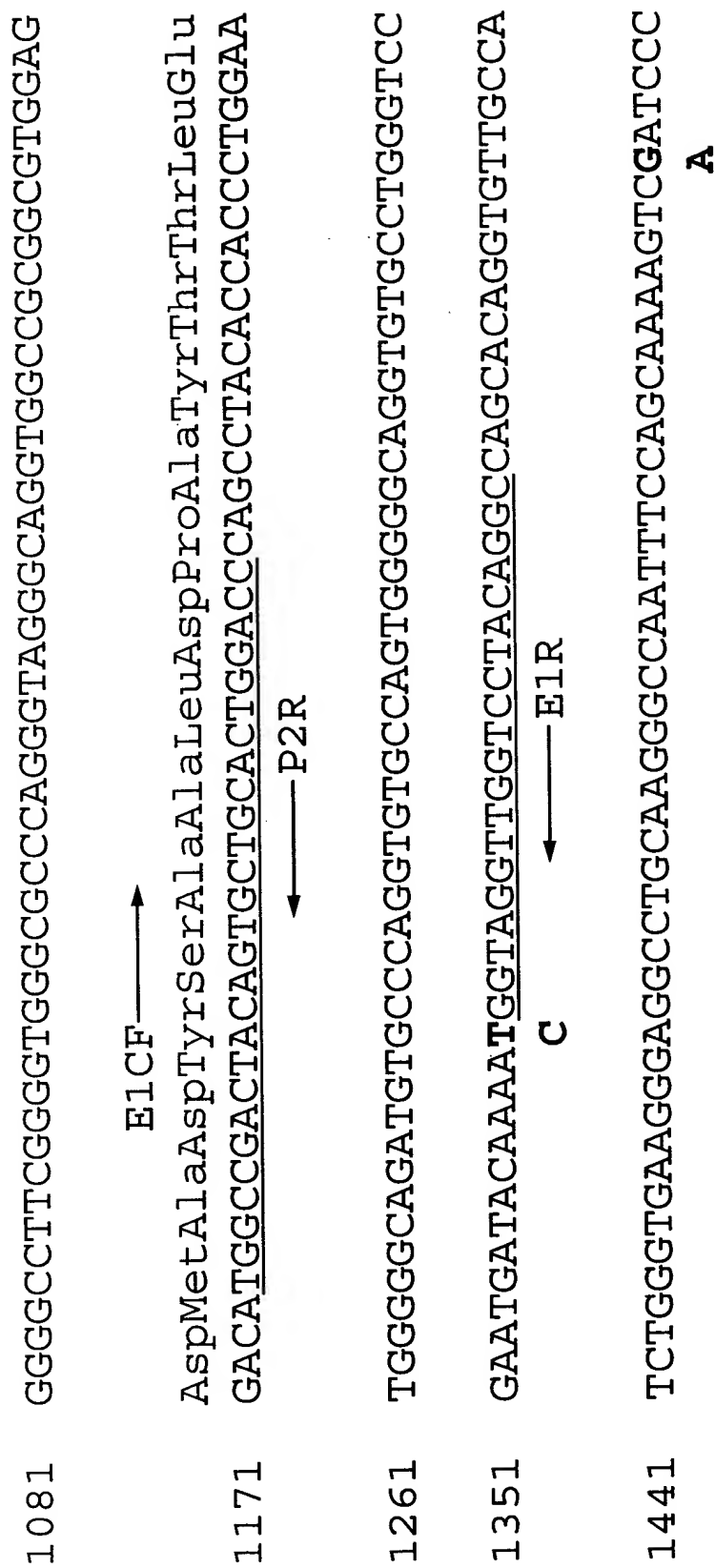


FIG. 28C-1



1

M R L S K T L V D Met
GCAGGAGAAATGCGACTCTCCAAAACCCCTCGTCGACATG

PheGluAsnValGlnValLeuThrMetGlyAsnG(ly)³⁰
TTTGAGAAATGTGCAGGTGTTGACGATGGGCAATG GTAGG

AGGAGCAGATCTTTGGCACTCAACTTTGGGTGGGAGGA

AGTGAAGCCCATGTGCCCCAGGCACAGTGATCACAGGCAT

Exon 1C (G)lyProSerSerProHisCysLeuT
GGCTATTCTCTCCAG GCCCTTCCAGTCCCTCACTGCCTCA

FIG. 28C-2



hrValAlaLeuGlyAlaTrpHisSerAspMetMet
1531 CAGTGGCTCTGCTTGGCGCTTGGCACAGTGACATGATG GTGAG
1621 TCGTGAACCCCTTGGGCCCTAGGTTCAAGAGACGGCAAGGGATG
1711 TGTCTTTGGGACTTTCCTAGGAAATGAAATTGGCACTTAGGGA
1801 CACTGTGTGTGTGTGTGCGTTCGTGTGTGATAGTGAGTTTC
1891 ATATGTGTGTTTCATTGTCTCTGTGTGTGAGTTCGGGTCTATT
1981 GCCCGTTGATCTTGCTTATGTATGTAAGTGTGTATGTGTGTG

FIG. 28D-1



CTCCCCCTTGGTGCCAGCTCCAGCGATTCAGCCCAGCACGGCCCCCT

←———— E1CR

TTGTATCCCTGGAGATGGTGGTTGGAGACATAACCGCATTTCTCGG

AAATGGAGCTCTCAGGGAAGTTTGTCTAACTACGAAGCCAACTCAG

CATGTAGGTTGTATGGGTGGGTGATGCCCTTCAGGAACCCATTGTC

TTCCCTTTGTATTTCATTGAGTGGGTCTGTGTTTGTGTCTTAGGAGTT

TACTTGTCTGTGGATGTTTGTACATGTGTGTGTGTGTGCGGGT

FIG. 28D-2



E1BF →
2071 CATAGAGCACATGCGTTTGTGTCATGCGGACCTGTTGGAGTGCCCC
2161 CATATTGTACCTGCTGTGTATATATGCAGTTCCCTGTGCTGCG
2251 TGCAGGACTCTGTTGTTGCCACTCACCAAGTGAGATTCAATCA
euAlaArgLeuArgHisProLeuArgHisHisTrpSerIleSer
2341 TCGCCAGATTGAGGCATCCCCCTCCGACATCACTGGAGCATATCT

FIG. 28E-1



TGTTCTTCCCTGCATCTTTATCCTGTATGGGCGTTTGTGCGTGCC

GGCGGGGTCAGCGGTCTCTGTGTGCACGACTGCACAGACCCAAA

A

Exon 1B IleLeuLeuProLeuArgL
GCAACATGTCCGTTTGTCTCTGTGAGCAG ATTTTGTGCGCGTGCCTC

GlyGlyValAspSerSerProGlnGlyA(sp)
GGAGGGTGGACAGTTCTCCACAGGGAG GTAGGGGAAAAGAGGAGG
G

FIG. 28E-2



2431 CCCGAAACCCCTCCTGGAGGGAAGAGCCCCCATCGGTCCCAGG
2521 CACCCTGCTTCCTTCTGTGTCTTGGAGCCACTCAGCCAGTATG
2611 AGGGTGAGGAGGCAGCTGCTGGGCACTGCTTGTGTCAGCTCA
2701 ATGTCACCTCCCCCTATCCTGGCTTCTGTATCTTCTACAAACA
2791 TGAGGACCACGCCAGGAGCGCAAGGCAAAAACACACAGAGAT
2881 CACCCAGAAGGTGGCCAGGTTTTCATGCCTTCCTAGAGAAAG
2971 AAGTCTGTGAAGTCACAACAGCCCCAGTTTACAGATGTGAAA

FIG. 28F-1

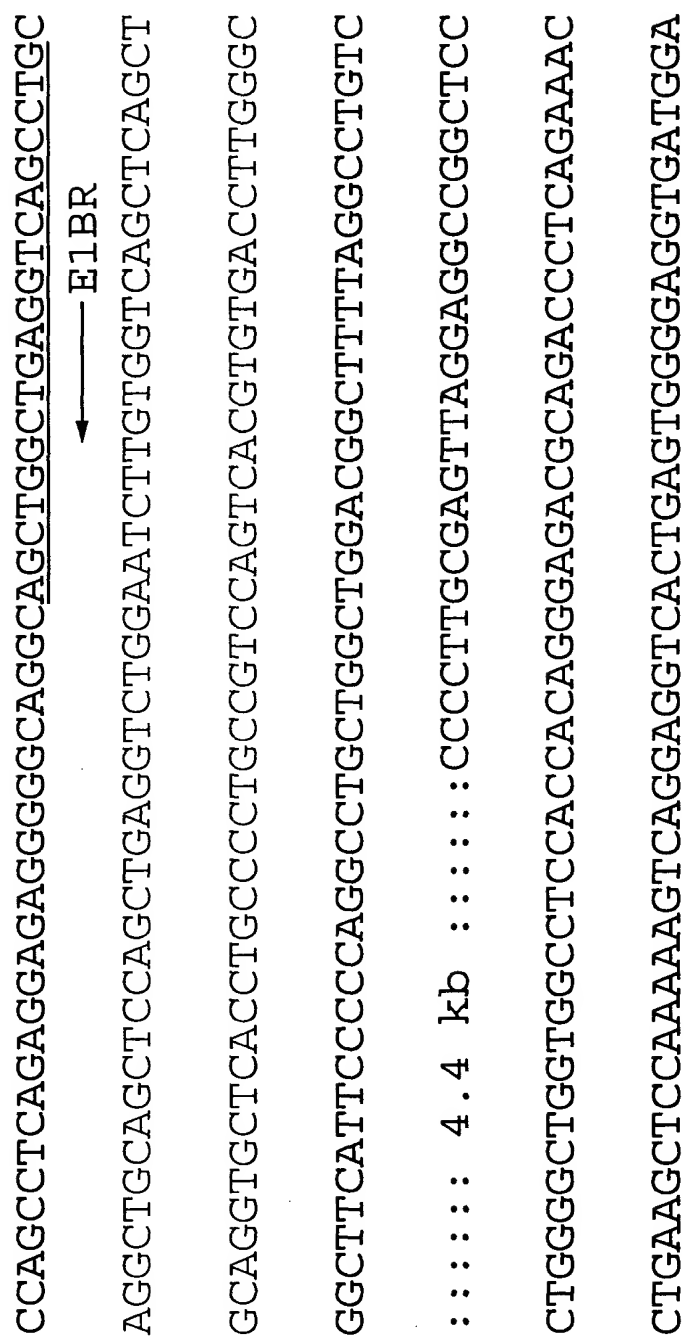


FIG. 28F-2



3061 GTGGGAACAGCCCCAGATCTGGCTGAGGCCGAAGCCCTGGAGA
Exon 2 30 (A) spThrSerProSer
3151 AAGCCTCACTCCCTTCTCTCCTGGCGCAG ACACGTCCCCCATGA
T
uCysAlaIleCysGlyAspArgAlaThrGlyLySHisTyrGly
3241 GTGTGCCATCTGCGGGACCGGGCCACGGGCAACACTACGGT
gLyAsnHisMetTyrSerCysAr (g) 88
3331 GAAGAACCACATGTACTCCTGCAG GTGAGGAGCCTCAATTCT
← E2R
3421 TTCTCCCTGAGTGGTAGGTCCCAGAGACAGCTGCCCTTCAGGG

FIG. 28G-1



E2F →

GAGATCCCCGCAAGGCTCCCTTAGATGCCCTGACATTCTGTCTTCCTG

T

erGluGlyThrAsnLeuAsnAlaProAsnSerLeuGlyValSerAlaLe
GAGAAGGCACCAACCTCAACGCGCCCAACAGCCTGGGTGTCAGCGCCCT

AlaSerSerCysAspGlyCysLysGlyPhePheArgArgSerValAr
GCCTCGAGCTGTGACGGCTGCAAGGGCTTCTTCCGGAGGAGCGTGCG

CTTCAGCTGGGAAATGGGCACACTTGGGCTCATGGCCCCAAGGTCCTGTC

GGCCTTCAAGGCTCTTCTGGTTTGTGTAAGAAAGACTTTGTGAATCCAAGA

FIG. 28G-2



3511 AGAGCATCTATTCTAGGAACCACATTTACTGATCATCAAGCTA
3601 AGTCTTTGTGTGTAATTAC::::: 1.6 kb ::::::GTAC
3691 CGACCCAGGACCACATGTTGCCCTCTCTGAGCCTCAGTTTCCCC
3781 TCCAGCTCCTGGTGGGTTCAAGAGAGAACTCCCGGGATGAAGA
E3F →
3871 GTTCTGTCCCTAAGAGGAGGAAGTTGTGTCTTCTCCATCCAACC

FIG. 28H-1



CTGGCTGCCGTTATTGAGCTCTTATCATATGCCAGGCACAATACTA
TCCAGAGGTCAAGGTTCCCAACTCAGCTCTAACACCAACCAGCAGAG
ATGTTTAGCAGGACAGGACTGGGCTCTTAGAGAGTTCATAGCACCTT
GATGAGGCACTGAGGTTGGGGGTCAACTGGATAGCCAGGGCCCTA

88

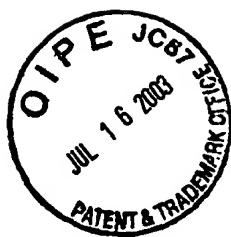
Exon 3 (Ar) gPheSerArgGlnCysValValAspLysA
ATCCAAAGCCCTCCCCAG ATTAGCCGGCAGTGCGTGGTGGACAAAG

FIG. 28H-2



spLysArgAsnGlnCysArgTyrCysArgLeuLys
3691 ACAAGAGGAACCAAGTGCCCGCTACTGCAGGCTCAAG
4051 ACCACCACTGCCCCACCTGCACCCACAGCTCCCCGAC
4141 ACTGGCTAATGGCTGAGAAGAGGGAGGCCCTGGAAAT
4231 5.9 kb ::TCCCCACTCCTCATCAGTCACAGACACCC

FIG. 28I-1



120 (A) laValGlnAsnGluArgAsp**Arg**IleSerThrArgArgSer
4321 AG CCGTCCAGAAATGAGCGGACCGGATCAGCACTCGAAGGTCA
aGluValLeuSerArgGln¹⁵⁵ T(R127W) (T/I130)
4411 GGAGGTCCTGTCCCGACAG GTACCGGGTGATCCTGCCACCCA
4501 TTCTCCCCAGCCAGGCCCTGGAGCAGCTGACGGGAGGGGCTCA
4591 GCAGCAAGGCAGGAATCGAACCTGGCGCCCTGGGGCACTTCT
4681 CTTCACTGAGGGCCTGCGATCAGCTCAGCTCCGAGAGAACAGAG

← E4R

FIG. 28J-1



SerTyrGluAspSerSerLeuPheSerIleAsnAlaLeuLeuGlnAl
AGCTATGAGACAGCAGCCTGCCCTCCATCAATGGGCTCCTGCAGGC

CCCAGGGATCCCCACACTACAGAGGAGCTCACCTCCTCCACCTCCA

GATATTACAGAAGGGACACTGAGTGCGGTTTCACATGGCCCCAGTTT

AATTCATCCTACTGCCCTGCATCCACAGGCCAAGCAGAGTCTTCAC

CAGTGGCTCAGTGGAGAGAGGTGGCAAAGTGGGGCCAGCCCCTTCC

FIG. 28J-2



4771 CTTGCTGAGTGACCTTGGGCAAGTCACAGCACCTCTCTGA
4861 CTCCTCTAAGGCTGACAGACTCCTTGGGGCTCTAAAGCTG
4951 CCGTTTTTACCCCTGAGCTTCCTTCAGAGCTGGAGGGCACC
E5F →
5041 AGGGACAGAGAAATGCGGGAGGGCCCGGACATCTCCAGCA
nGlyAspIleArgAlaLysLysIleAlaSerIleAlaAsp
5131 CGGCGACATTGCGGCGAAGAAGATTGCCAGCATCGCAGAT

FIG. 28K-1



GCCATGGTTGCCTCATTTGTCAGAAAGGATGATGATTTTGTGCCCTGCTT

::::: 1.0 kb :::::TTCTCCCTCATCCCTGCCCTCCTCCCTCCCT

CACTATCCAGCCCCACATCTGATTCCAGGAGGGGCTCTGTGC

Exon 5 156 IleThrSerProValSerGlyIleAs
TTTTCTTCCCTGTATCTCTCGAAG ATCACCTCCCCCGTCTCCGGGATCAA

ValCysGluSerMetLysGluGlnLeuLeuValLeuValGluTrpAlaLy
GTGTGTGAGTCCATGAAGGAGCAGCTGCTGGTTCTCGTTGAGTGGGCCAA

FIG. 28K-2

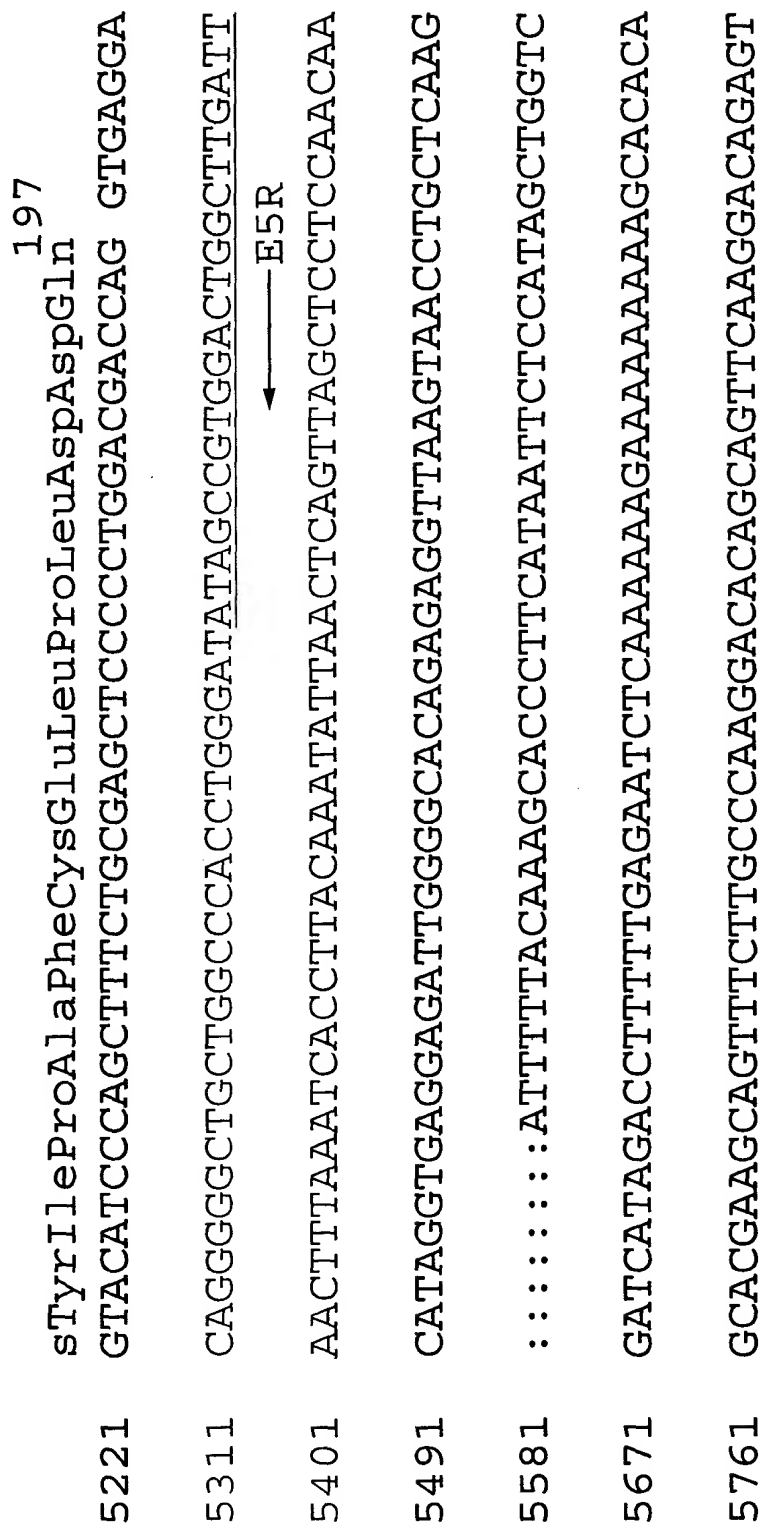


FIG. 28L-1



TGGCGTGATGGTGGGCAGTAGTGGGCAGTGGCGGGGCAGC
TTATTTTATTAAACAAAATATGTAGTGCACACACGTGTCTGA
CTCTATGAGGTAGGTACTAAGTACTATTATTACTGCCATCT
GTCACATAGCTACTATCCAGCATAGCTGGG::: 4.3 kb
CATGGGTGGGAATTGGGACCCACAGTTTGGAACTTTTGG
GAATGTTGCTTACAGTTTCATCAGGCACACAGAAGAGGCCCA
CAGCGGAGGTCTCTCAGCTCTGAGCACATGTTCTTCCCT

FIG. 28L-2



5851 TCCAGGTTCTAGTTTATGGGTAGTAGTTTATG
E6F →
5941 GCCAGCGTCACTGAGTTGGCTACGGGCAGCCTTC
rgAlaHisAlaGlyGluHisLeuLeuGlyAla
6031 GAGCCATGCTGGCGAGCACCTGCTGCTCGGAGCC
6121 GCCCTGGCCAGGGCTCCAGGGAGGGTATGCCTAG
6211 CTAGTCAGGAGTGGCCCTGTCTCAGGCTTGCA
6301 GTGGATGCAAGTCACCAAAATCCCAGCATTTGAAG

FIG. 28M-1



ATGCCCATTTACAGTTCAGGCAGGTAGAGGCAGAGGGAGCATTAAGCTGACTT

198 ValAlaLeuLeuA
Exon 6
CCAAGGTACAGATGGCAAACACTGTTCCCTTCTCTCTTTTCAG GTGGCCCTGCTCA

237
ThrLysArgSerMetValPheLysAspValLeuLeuLeuG(ly)
ACCAAGAGATCCATGGTGTTC AAGGACGTGCTGCTCCTAG GTGAGGCGGCTGCCT

CATGGCACTCACCCAGGCAAGGAGATTCACATGGTGGCATGCAAGGGTGAGGGAGA
← E6R
TGGAGGGCTCCAGGACTCAGTTTTCAACTGGGTACCCCACTCAGATGCAAGGAAAT

TCAGAGCACGATCAGGGTTATCCCTGGAAATTACCTGTGCATCCTTTTCTTTTGA

FIG. 28M-2



6391 CAGAGTCTTGCTCTGTCACTCAGGCTGGAGTGCAATGATGTGA
6481 ATGCTATGAGGAGCTCGATTATTATCTCATCTTATAGATA
6571 AGCTATCAGGGCAGAGCCATTTAAGCAGGCAGTGCAGTTCC
6661 TTTGAATGTCAATCGATCTTGTGAGTCATGTTGGTAAATGGAGC
6751 CGGATGACTCAAGGCAGCTTATCTTCTGAATCTGGGCTCAGC
6841 CACAGGCACCAGCTATCTTGCCAACTTAAAGCCAAACTAGA
E7F →

FIG. 28N-1



::::: 1.4 kb :::::GCAACACTACCTATTTTAATATAACA
AGAAAAC TGAGGCACAGAGAGGTTAAGTAACTTATCCAAC TATAACC
AGAATCTGGTCCTTTAACTTGATGCTTTGGTGCCTATCAGGTGACC
TTGGGTCATGTGAAAGAGGTCCTAGAAAGCCAAGTTCCAAGCTCAGC
TTCCTTACCTGTGAAATGGGAGTCACCATCCCTGCAGGTCCTCCTCC
GGAGAGGGTCAACCCAAGGTGACTTCCCATCCTCCCTCCCTCCCAA

FIG. 28N-2



237

Exon 7 (G)lyAsnAspTyrIleValProArgHisCysProGluLeuAla
6931 CCCTTCCAG GCAATGACTACATTGTCCCTCGGCACTGCCCCGGAGCTGGCG

alLeuProPhe**G**lnGluLeuGlnIleAspAspAsnGluTyrAlaTyrLeuL
7021 TGCTGCCCTTCCAGGAGCTGCAGATCGATGACAAATGAGTATGCCCTACCTCA

T (Q268X) C

7111 CCTAAGCCATCCCTGACTCTCTCTCCAGAACGCTCTGCCAGACTTCTCCT

←E7R

7201 TAACGACAGCCAGGAGAGGCCGTTTTCATTTAACAGATGAGGCAAGTCAA

7291 CTGTAATCCCATCACTTTGGGAGGCTGAGGCGGGGATCACCTGAGGTC

FIG. 280-1



GluMetSerArgValSerIleArgIleLeuAspGluLeuV
GAGATGAGCCGGGTGTCATACGCATCCTTGACGAGCTGG

ysAlaIleIlePhePheAspProA (sp) 289

AAGCCATCATCTTCTTGACCCAG GTACAGTGCACACCT

ATTGGGTTCTGTACACTGAGTTCACAGCCTCATCTCATGT

GATTGAAGAGACAATAATGGCCGGGCGCAGTGGCTCACAC

AGGGGTCAAGATGAGCCTGGCTAACATGGAGAAACCCCAT

FIG. 280-2



7381 CTCTACTTAAAA::: 1.5 kb :::::GT
7471 CTGGGTTTCCCCCGTGTGTAGATGAGGCGGTTGC
7561 CTTCTGGTTTAGTGCTTTAGGAAATGTGGCAGAA
7651 TGAGGTCCCTGAATCCTTG TGCCCCACACTGCTGA
7741 CCAGCTGGACCCCTGCTGCCCCCTCCCTTGCCCCACCC

FIG. 28P-1



GGCTCTGCCAACAACTGGCTGTGCGACCCAGGACAAGTCCTATCTTTTGCACTGTGT

TAGTGCTTATTGGATGCATTCTCAAGTCCCGCCCTCCATCTCCTATTCCCCCTCT

ATCTTTTCTGCCCTGTGTCTAGGAAATCATATAATTCAATGCTGGCGTACCCCTGGTTGT

E8F →

AGACTCCTTGTGTGACACAAAGTCAGGGGACATCTGGGTCTTGACTCCCCAGATGCT

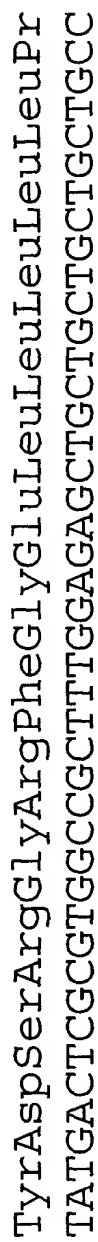
Exon 8 289 (A) spAlaLysGlyLeuSerAspProGlyLysIleLysArgLeuAr
TCTTCCATTGTAG ATGCCAAGGGGCTGAGCGATCCAGGGAAGATCAAGCGGCTGCG

FIG. 28P-2



gSerGlnValGlnValSerLeuGluAspTyrIleAsnAspArgGln
7831 TTCCCAGGTGCAGGTGAGCTTGGAGGACTACATCAACGACCGCCAG
oThrLeuGluSerIleThrTrpGlnMetIleGluGlnIleGlnPhe
7921 CACCTTGCAGAGCATCACCTGGCAGATGATCGAGCAGATCCAGTTC
uMetLeuLeuGlyG(ly)³⁶⁸
8011 GATGCTGCTGGGAG G P C Q A Q E G R G W
CCTCAGCTCCTTGGCTTCCCCACTGTGCCGCTTTGGCAAGTTGCT
8101 L S S L A S P L C R F G Q V A

FIG. 28Q-1



IleLysLeuPheGlyMetAlaLysIleAspAsnLeuLeuGlnGlu
ATCAAGCTCTTCGGCATGGCCAAAGATTGACAACCTGTTCAGGA

GAGTGGGACTCCCGAGAGACAGGCCTCACACAGTGAGCTCACC
S G D S P G D R P H T V S S P

TAACTGTCTGTGCCCTCAGTTTCCTCACCAGAAATGGGAACA

FIG. 28Q-2



8191 AGGCAATGGTCTATTGTTCAGGCACCGAGAACCTAGCACGTGCCAGTC
8281 TGCCCTCGGGAGGCTGTGTGTGTGAGTATGTATGGATGCGTGGATA
8371 CCTCACATTTTATGATTTTGAAATAACAGGTAATATGA::: 4.4
8461 GGCTGCAGCAGAGATGTGGGGGATGAGGCTGAAAGGTGAGCGGGACCA
8551 TTGATTACATCCATTATGTACTATGTGACCAATACATTACTCATTTAGA

FIG. 28R-1



ACTGTTCTAAGTGTGGCAATTTCAGCAAGAACAAGATCTT

TCTGTGTATATGCCCGTATGTGCGTGCAATGTGTATATAAAG

kb :::::GGGACACATAGATGCTATAAGTAGGTCAGTT

AATGGTTGAAGGACTTGCACTCCAAGGAGCTTTGAGAGCCA

ACATTACGTGATCTCAGAGCTTCCTTATATGCACCTTGTT

FIG. 28R-2



8641 CCTTCAACTCAGTTTGTTCCTCTTGTTTGGGGT
8731 CTAACCCAGGAATAGGTACCCAACAGGCACTGCCAATA
8821 TGAGGTCTGCATCCAGACTCTCCATCCTGATCGACCT
isProHisLeuMetGlnGluHisMetGlyThrAsnVal
8911 ACCCTCACCTGATGCAGGAACATATGGGAACCAACGTC
rpProArgProArgGlyGlnAlaA(1a)⁴¹⁹
9001 GGCCCGACCCAGGGACAGGCAG GTGGGCAAACTCT

FIG. 28S-1



CCTCTTAACACCCCTCATGAAGTCTATAGATGGGAATGGTACACCCCTAGTTTA

E9F →

TTGGATGGGCTGGTTGATTGGCCACGCCCTGAGGAAGATGGCGTCCCAAGGCC

Exon 9³⁶⁸ (G) lySerProSerAspAlaProHisAlaHisHisProLeuH
TCTCTACCTGCAG GGTCCCCAGCGATGCACCCCATGCCCCACCCCTGC

IleValAlaAsnThrMetProThrHisLeuSerAsnGlyGlnMetCysGluT
ATCGTTGCCAACACAAATGCCCACTCACCTCAGCAACGGACAGATGTGTGAGT

GGGATTTTACCTTGCAAAGGGTGAGGATGGGGCTTAAGACAGGAGGCAGGAGA

FIG. 28S-2

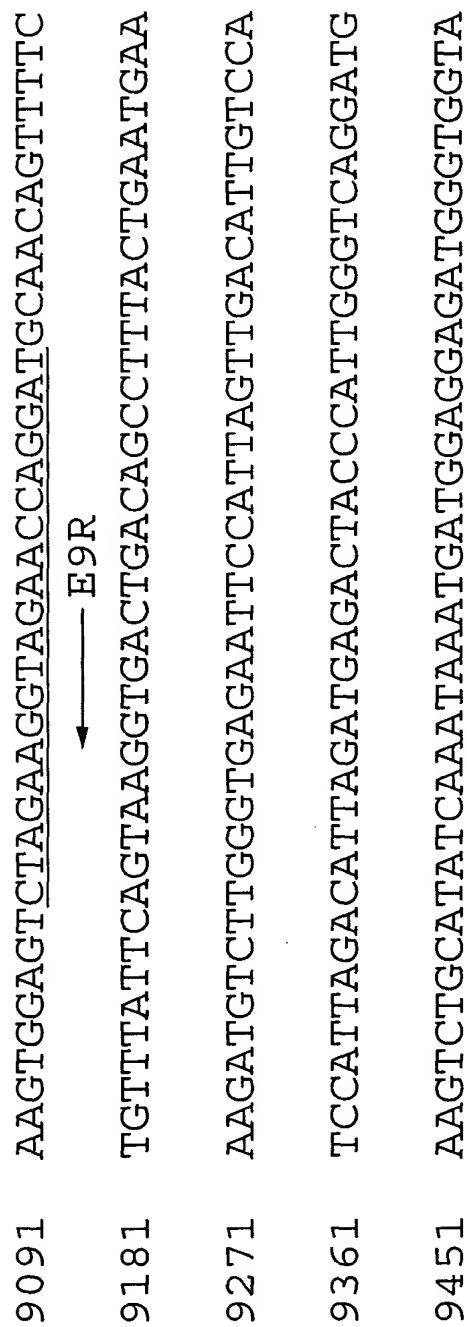


FIG. 28T-1



TGGGTTCCAGGTTAGGGAATAAAGGGCAAGATTGTCCATTTTGTTGAGGC
GCCATTGTTGGGATGAGGCAATCCACTGGATGAGGTAACCCATTGGGTG
TTAAGTAAAGTGGTCATTGAAGTAAGGCTGCACAGTTGGGTAAGGCTA
TCTGCTGGGCTA::::: 1.4 kb :::::TTTGGGAGAAGCAGTCC
GGACCTTCCAGACCTCATAAAACTTAGGCTTTATGATCTGGGACTCACA

FIG. 28T-2



9541 GAAGGTTGAGCAATAAAAGACCTTAGGGATTATCTGGCTTAATTAATTC

E10F →

9631 GGTGGAGGGAGAACTTCCCGGGCTCTTCATTTACTCCCAAAAGGCT

419 (A) laThrProGluThrProGlnProSerProProGlyGlySerGlySer
9721 AG CCACCCCTGAGACCCACAGCCCTCACCGCAGGTGGCTCAGGGTCT

lLysProLeuSerAlaIleProGlnProThrIleThrLysGlnGluVal
9811 CAAGCCCTCTCTGCCATCCCCAGCCGACCATCACCAAGCAGGAAGTT

FIG. 28U-1



TCATTTTATAGAGGAAGAAATTAAAGTCAAGGTGGGCAG

Exon 10

GGAATTTTGAGCAGCCCCTGTCTGTCTGTTGTCCCTTCC

GluProTyrLysLeuLeuProGlyAlaValAlaThrIleVal
GAGCCCTATAAGCTCCTGCCGGGAGCCGTCGCCACAATCGT

IleOP⁴⁶⁵

ATCTAGCAAGCCGCTGGGGCTTGGGGGCTCCACTGGCTCCC

FIG. 28U-2



AAAGGAAGACGTGATGCCAGGACCAGTCCAGAGCAGGAATGGGAAG
CCCTGACGCCCTGCTCTGATAACAAGACTTTGACTTTGGGGGAGACCT
ACCTTACCTTCATCCATGTCCAACCCCGACTTCATCCCCAAGGAC

FIG. 28V-2